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Factors Involved in Prostate Cancer Disparity in African Americans: from Health System to Molecular Mechanisms

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Abstract

The high incident and mortality rate in African American patients reflects the racial disparity in prostate cancer (PCa). African American men are affected by several non-biological and biological factors that increase their susceptibility to develop aggressive PCa compared with Caucasian men. Here, we provide a general view of some factors that impact the outcome, focusing on socio-economic factors and with more detail on a molecular perspective covering the mutations, polymorphisms, or epigenetic changes that influence cell proliferation/death balance, androgen pathway and immune response involved in PCa racial disparity. Moreover, we provide an overview of how non-biological and biological factors are interconnected in properly managing diseases.

Keywords: Prostate Cancer, Cancer Disparity, Androgen Receptor.

Introduction

Prostate cancer (PCa) is the most common cancer diagnosed in men and the fifth leading cause of death worldwide [1]. The incidence among African American (AA) men in the US is 60% higher compared with their Caucasian (CA) counterparts, and the mortality rate is 2.5-fold increased [2, 3]. AA men present at the diagnosis with more aggressive disease, worst prognosis, and worst therapeutic response with a higher risk of recurrence [4-6]. In addition, AA patients exhibit more severe side effects of conventional therapies than their CA counterparts [7]. Although socio-cultural disparities are often associated with PCa outcomes in AA patients, several other biological factors are also involved.

Among the non-biological factors that impact PCa treatment and outcome are socioeconomic status, lack of access to adequate health, physician-patient barrier communication, lifestyle, and environment. Biological factors, including germline polymorphisms, family history, hormonal levels, and molecular alterations, contribute to race-specific prostate cancer development, incidence, and clinical outcome.

Socio-Cultural Factors in Racial Disparities of Prostate Cancer

One of the first barriers involved in the correct prevention, diagnosis, and treatment of PCa, in general, is the lack of knowledge related to genitourinary health and the risk factors involved in the development of PCa, including age, family history of PCa, sexually transmitted disease history, smoking, diet, among others according to American Cancer Society (cancer.org). In addition to this, other sociocultural factors involved in the PCa disparity in

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AA men include poor interpersonal communication between physicians and patients, including physicians' failure to provide necessary information and racism, patients' distrust in the health care system, and lack of adherence to therapy. Even if the barriers mentioned above are overcome, the socioeconomic status of the patients impact directly in the affordability of the treatment, and consequent outcome; indeed, socioeconomic status in AA patients diagnosed with PCa is directly associated with increased mortality and morbidity [8, 9]. Furthermore, fear of diagnosis and treatment strategies and poor health consciousness contribute to the late diagnosis. These and other factors were reviewed in-depth elsewhere [10]. Socio-cultural and biological factors influence dietary habits; however, the exact molecular mechanisms of how these act remain unclear. In particular, vitamin D deficiency is associated with increased susceptibility to developing prostate cancer in AA men [11]. On the other hand, high calcium intake is associated with aggressiveness of PCa [12].

Molecular Basis of Racial Disparities in Prostate Cancer

Molecular factors such as genetic modifications, including gene polymorphism and mutations, epigenetic alterations, dysregulation of miRNAs, and over-activation of several signaling pathways, are involved in PCa disparities [13].

Genetic Variants

Since PCa is one of the most recognizable inherited malignancies associated with hereditary breast and ovarian cancer (HBOC) and Lynch syndromes (LS), some germline polymorphisms and mutations are involved in the disparity susceptibility to develop PCa in AA men as described below:

Chromosome 8. The deletion of the short arm of chromosome 8 is frequently found in prostatic intraepithelial neoplasia and adenocarcinomas, which participate in prostate cancer carcinogenesis [14, 15]. Although the exact mechanisms by which alterations of 8q24 participate in PCa development are unclear, some polymorphisms may influence the expression of neighbor genes, such as c-MYC [16]. The allelic variant of 8q24 is reported to be associated with the risk of PCa in young AA men [17], and alteration of 8q24 is associated with hereditary PCa in AA men.

MSR1. Macrophage scavenger receptor 1 (MSR1), also known as CD204, is a multifunctional receptor that binds modified self- and pathogen-associated antigens. MSR1 plays an important role in maintaining immunological tolerance [18]. MSR1 gene is associated with germ-line alterations in 8p and prostate carcinogenesis. Several variants of MSR1 are found to be associated with PCa susceptibility in AA men [19]. A specific mutation in the MSR1 gene that results in 520G>T is associated with PCa, and AA men exhibit a high frequency of this mutation [20]. However, there is limited support for an association in AA men.

HPC1. Hereditary prostate cancer 1 is localized at 1q24-31; several studies suggest that HPC1 increases the risk of hereditary PCa development in AA men [21, 22]. Furthermore, in the loci of HPC have been identified several candidates that contribute to susceptibility, such as HPCX at Xq27-28 and RNASEL at 1q25 [23]. While HPCX variants are associated with an increased risk of PCa, variants in RNASEL contribute to susceptibility to the early onset of the hereditary form of PCa [23].

Apoptotic genes: Cell cycle regulation is disrupted in cancer by the imbalance between cell growth and cell death; many genes related to apoptotic functions are altered in PCa as described as follows:

Anti-apoptotic BCL2. BCL2 protein plays a crucial role in cancer development and progression and exhibits an anti-apoptotic effect in cancer cells. BCL2 expression in PCa is associated with increased resistance to therapies. AA men present higher expression of BCL2 compared with their CA counterparts. Thus, the overexpression of BCL2 in AA men may participate in prostate tumor growth and aggressiveness [24]. It was reported that a functional single nucleotide polymorphism (c.-938C>A, r*s2279115*) in the inhibitory P2 promoter of *BCL2* results in altered transcription factor binding and expression [25]. While the BCL2 -938C allele was significantly associated with increased P2 promoter activity, which results in decreased BCL2 transcriptional activity and protein expression [26, 27], the BCL2-938 CC genotype (CA allele +AA allele) is associated with an increased risk of biochemical recurrence [28]. In 2014, Renner et al., showed a strong association between the BCL2-938 CC genotype and reduced survival in PCa patients [29]. However, the study by Bachmann et al., reported an association of the BCL2-938 AA allele with a worse outcome in PCa patients [26]. The C allele is the most common in AA populations. The cause of this discrepancy is unclear.

MDM2. This ubiquitin ligase protein is involved in several functions, such as promoting the degradation of the tumor suppressor p53, DNA repair, and apoptosis [30, 31]. MDM2 is significantly highly expressed in CA patients compared with AA, and the overexpression in PCa is associated with cancer progression in a mechanism dependent on p53 degradation [32]. However, the expression in AA patients is associated with poor prognosis. Bond et al., reported a single nucleotide polymorphism (SNP309), which enhances transcriptional activation of MDM2 downregulating p53 pathway [33]. In addition, Wang et al., reported no difference in the expression level of SNP309 between AA and CA patients [34]. Still, interestingly, in a meta-analysis performed by Yang et al., they showed that the MDM2 309G variant was markedly

associated with a low risk of developing PCa and slower clinical progression in CA men [35]. Thus, some controversies need to be studied more deeply.

Caveolin-1. This structural protein is involved in tumor progression and metastasis and was reported to participate actively in radio-resistance acquisition [36]. Since caveolin-1 is significantly upregulated in PCa cells and mediates downstream signaling mechanisms related to the development of aggressive PCa, caveolin-1 was proposed as a prognostic biomarker to monitor tumor radioresistance [36]. Furthermore, caveolin-1 is involved in the suppression of apoptosis by suppressing c-MYC. In addition, Caveolin-1 was found overexpressed in prostate adenocarcinoma cells and is implicated in the progression of androgen-dependent PCa to androgen-independent [37]. It is known that a high level of caveolin-1 is associated with poor treatment outcomes [36]. AA men diagnosed with PCa exhibit a significant increment in the level of caveolin-1 compared with their CA counterparts [38]. Although caveolin-1 polymorphism rs7804372 is associated with the risk of several types of cancer (10.4236/ym.2020.43020), there is no current information on AA risk to PCa with this polymorphism.

Growth factors and receptors: As a counterpart to balance cell death, cell survival, and proliferation are driven by several growth factors**.** Epidermal growth factor and receptor (EGFR) and EPH receptor (EPHB2) are the most common receptors involved in the racial disparity of PCa. AA men exhibit a higher level of IGF-1 and lower levels of IGFB-3 that may participate in tumor growth and progression. IGF and ligands are effectors of AKT signaling, activating PCa development, metastasis, and anti-apoptosis [39].

EGFR. The EGFR signaling pathway is one of the most critical pathways to PCa development. This pathway is implicated in the progression of PCa from androgen-dependent to androgen-independent and is associated with metastasis [40]. Several studies have identified racial differences in dinucleotide (CA)n repeat polymorphisms in intron 1 of the gene [41]. The number of CA repeats is related to transcriptional activity. Thus, the longer allele is associated with reduced protein expression. In contrast, shorter alleles, which are more frequent in AA men, are associated with overexpression and PCa development [42].

EPHB2. The gene encodes a tyrosine kinase receptor and is a tumor suppressor gene. Somatic inactivating mutations occur in approximately 10% of sporadic tumors. The nonsense mutation K1019X (3055A-T) is more frequently found in AA men and is associated with an increased risk of PCa development. [43].

Androgens pathway. Several studies have shown that sex steroid hormone levels are also implicated in the racial disparities in PCa. These studies have shown that AA men exhibit approximately 11-15% higher levels of testosterone, 13% higher free testosterone, and higher activity of 5-alpha reductase than CA men [44-46]. Although there is no established relationship between the level of circulating androgens and PCa, the level of androgens is considered a risk factor. Furthermore, mutation or alteration in several genes involved in androgen biosynthesis may contribute to the racial disparity.

Androgen receptors. Androgens bind androgen receptor (AR), inducing several androgen-regulated genes required for prostate cell growth and maintenance. AR is a transcription factor, a gene mapped in Xq11-12 and composed of 8 exons. Exon 1 encodes the N-terminal domain, which is a transactivation domain. This domain controls the transcriptional activation of the receptor and exhibits several highly repetitive DNA sequences. Polymorphic trinucleotide repeats (CAG) are associated with PCa disparity. One study performed in 587 cases of PCa compared with 588 controls, which involved 95% of CA patients, showed that shorter CAG repeat sequence was associated with metastasis and high grade of the disease [47]. In addition, Do et al., analyzed CAG repeat length in 109 cases of PCa and found that the median CAG repeat length was 25 in patients with early status of PCa, while in advanced status, the CAG repeat length was present between 22-23. Further, they found a significant correlation between these CAG repeats and the age at onset of the disease, suggesting that these repeats may be associated with an increased risk of developing PCa [48]. On the other hand, Sartor et al., analyzed the presence of these repeats in 130 CA and 65 AA average men, finding that AA men exhibit significantly shorter repeats than their CA counterparts [49]. Thus, shorter CAG repeats may explain the occurrence at a younger age and the rapid progression of PCa in AA men.

Genes involved in androgen biosynthesis. Polymorphism in genes involved in androgen biosynthesis and metabolism may modify the expression of androgen levels, contributing to racial disparity. Some of these polymorphism genes are the following:

CYP17. The *CYP17* gene is located on chromosome 10 and encodes the cytochrome P450c17a enzyme, which participates in the steroid biosynthesis pathway [50]. The polymorphic T-to-C substitution in the 5' promoter region results in A1(T) and A2(C) alleles [51]. One study conducted by Wadelius et al., evaluated the association between the polymorphism in the CYP17 gene and prostate cancer in 178 CA patients diagnosed with PCa using as control 160 age-matched control individuals. After evaluating the presence of the polymorphism in blood samples, they reported the frequency of the CYP17 A1 allele was significantly higher in prostate cancer patients [52]. Supporting the results

as mentioned earlier, Habuchi et al., published a study performed in a Japanese population that included 252 prostate cancer patients, 202 benign prostatic hyperplasia (BPH) patients, and 131 male controls, which found that the A1 allele is associated with an increased risk of both prostate cancer and BPH, but not influence in the status of the disease [53]. Despite several studies reporting that the A1 allele is associated with an increased risk of PCa in CA and Japanese patients [52, 53], other studies show the opposite. Lunn et al., performed a study in 108 CA prostate cancer cases where they found that the A2 allele (genotype A1/A2 and A2/A2) was the most frequent in CA PCa patients compared with control urology patients [54]. Contrary to the report in CA, Ntais et al., by performing a meta-analysis of 10 studies that included 2404 patients with prostate cancer and 2755 controls, found that while the allele A2 seems not to affect the predisposition to develop PCa in CA people, in AA men the presence of A2 allele is associated with PCa development [55]. In addition, and supporting this finding, Kittles et al., by analyzing the presence of the A2 allele (genotype A1/A2 and A2/A2) in Nigerian (n=56), CA (n=74), and A-A (n=111) healthy male as a control found that AA men homozygous for the allele A2 present a higher risk to develop PCa [56]. Thus, the association is not conclusive.

CYP3A4. A germinal variant (A to G) in the 5' regulatory region of the gene determines the variant *CYP3A4-V*. One study conducted by Rebbeck et al., on 230 Caucasians shows that *CYP3A4-V* is associated with the development and aggressiveness of PCa in CA but not in AA men [57]. In AA men, the variant *CYP3A4 G* is more frequent and is associated with poor prognosis [58].

CYP19A1. The CYP19A1 gene is mapped in 15q21.1 and encodes the enzyme aromatase. At least 30 SNPs have been identified and associated with a high estradiol level in men's serum. The polymorphisms *rs2470152*, *rs12439137*, *rs3751592,* and *rs2470164* are associated with a high risk of PCa in both AA and CA. [59]. However, CA men bearing rs2470164 polymorphism present a higher risk.

SRD5A2. This gene encodes steroid 5-α reductase type 2, which converts testosterone to DHT and is exclusively expressed in the prostate [60]. SRD5A is highly polymorphic in AA men, and SRD5A2 TA repeats are exclusively present in high-risk AA men. Other variants, such as V89L and A49T, are involved in converting DHT from testosterone; the first variant decreases the production, while the second increases the production in AA men [61].

The HSD3B family, HSD3B1 and HSD3B2, encode 3β-hydroxysteroid dehydrogenase type 1 and 2, respectively. A notable variation that frequently occurs in prostate cancer is the N367T (rs10473003) polymorphism in HSD3B1. While this variation is more prevalent in CA than in AA, it does not significantly modify its activity compared with the wild type, underscoring its importance in prostate cancer genetics [62]. The presence of (TG)n(TA)n(CA)n dinucleotide repeats in the intron 3 of *HSD3B2* gene presence variation between racial populations, the longer sequences are associated with faster degradation of DHT. In contrast, the shorter alleles are associated with PCa risk and aggressiveness in CA men [63]. Two SNPs were reported in *HSD3B1* (*rs1819689* and *rs1538989*), which are more frequent in AA men and are associated with PCa in that racial population [59].

miRNAs. MicroRNAs are endogenous non-coding RNA that regulate gene expression. The correct regulation of the expression at transcriptional and post-transcriptional levels by miRNAs is required for the basic cellular process. These small sequences of oligonucleotides could function as a tumor suppressor or oncogenes according to their expression level [64, 65]. Since the miRNAs are specific to the type of cancer, tumor grade, and level of metastasis, miRNAs have the potential to be used as a stage-specific biomarker of cancer [66]. Some miRNAs such as (miR-21, miR-17-5P, miR-191, miR-29-b2, miR-223, miR-199-a1, miR-146, miR-181-b1, miR-20a, miR-32, miR-92-2) are up-regulated in PCa but also are up-regulated in other solid tumor. Thus, these miRNAs are not specific but belong to the signatures of some solid cancers [67]. Recently, Sharma et al., published a review identifying a panel of miRNAs differentially expressed in PCa. These miRNAs include miR-141, miR-375, miR-221, and miR-21 and are the most common dysregulated miRNAs in prostate cancer independent of the racial disparity [66]. The role of these miRNAs in PCa is shown in Table 1. Calin et al., reported at least five miRNAs that are differentially expressed between AA and CA patients diagnosed with PCa (miR-26a, miR-30c-1, miR-1b-1, miR-219, and miR-301) [68]. In addition, Ren et al., working with a cohort of 27 cases of radical prostatectomy PCa samples, reported that the expression of miR-30c and miR-219 were downregulated in PCa, but miR-21 and miR-30c were significantly downregulated in PCa in AA cases compared with CA cases. They also found the downregulation of let-7c in PCa stroma cells was significantly associated with metastasis [69]. However, it is necessary to note the limited number of cases analyzed in the study. Another group using a combined platform intergraded by cancer cell lines, transgenic mice, and human tissue samples has shown that loss of miR-34b expression occurs in AA patients more frequently than in CA, and the loss of the expression is associated with PCa progression in a SOX2 dependent mechanism [70]. Working with the AA and CA cancer cell lines model, Theodore found that mir-26a is significantly expressed in AA compared with CA [71].

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miRNA	Expression in PCa	Androgen Receptor	Proliferation-metastasis	EMT	Apoptosis	Ref
141	Increased	Induces growth of CRCP	Promotes proliferation and stemness properties	Promoter and partial inhibitor by suppression of zeb1 and Vimentin	Inhibitor	[102-105]
375	Increased	Implicated in CRCP	Promotes proliferation, invasion and metastasis	Promoter and partial inhibitor by suppression of zeb1	No established	[106-108]
321	Increased	CRPC phenotype, NE differentiation, regulator of CRPC	Promotes proliferation, migration	No established	Promoter/ Inhibitor	[102, 109-113]
21	Increased	CRPC development	Promotes proliferation	No established	Promoter	[114-116]

Table 1: Common dysregulated miRNAs in prostate cancer

Epigenetic Changes

Epigenetic processes regulate gene expression, a reversible process that, contrary to mutation, consists of DNA methylation, modification of histones, chemical modification, and chromatin remodeling that result in changes in gene expression without modification of the DNA sequences—epigenetic process blockage of the access of transcriptional factors to the target genes promoter. Thus, genes are not able to be transcribed. Since the epigenetic changes are reversible, they allow the development of new opportunities for therapies to recover the initial condition. Several genes exhibit aberrant methylation in PCa. Among these genes are found *GSTP1*, *MGMT*, *CDH1*, *CD44*, *CDKN2A*, *APC*, *RARβ*, *RARRES1,* and *RASSF1*. *GSTP1* gene is localized in chromosome *11q13* and encodes glutathione S-transferase. Hypermethylation of *GSTP1* seems to be exclusive of PCa cells and is present at all stages of PCa. *MGMT* is localized in chromosome *10q23* and encodes DNA methyltransferase enzyme. Its methylation was reported in PCa patients and cell lines and is associated with carcinogenesis [72]. Since both enzymes are involved in cell detoxification and DNA repair, they may be involved in the genomic instability of the cells. *CDH1* gene is another gene hypermethylated in PCa, which encodes E-cadherin protein that participates in cell-cell adhesion. Hypermethylation of *CDH1* results in loss of E-cadherin expression, which is associated with metastasis development [73, 74]. *CD44* hypermethylation is found in 78% of patients diagnosed with PCa, a characteristic feature of epithelial-mesenchymal transition [74, 75]. *CCND2* promoter hypermethylation is found in 32% of PCa, and the high methylation level of the gene is correlated with tumor aggressiveness [75, 76]. APC protein encoded by the *APC* gene participates in cell cycling regulation, migration, and differentiation. The silencing of the APC protein product of promoter methylation is associated with high-grade and advanced stages of PCa [77]. Other genes were reported to be hypermethylated in PCa, such as the retinoic acid receptor (RARβ), RARRES1, and *RASSF1*, in which proteins are found in low levels and are involved in PCa development [78-80]. On the other hand, hypomethylation is associated with cancer metastasis and is frequently found in repetitive sequences of LINE-1 in PCa metastasis [81, 82]. Higher expression of urokinase plasminogen activator, heparanase, cytochrome p450s, WNT5A, S100P, and cysteine-rich intestinal protein 1 due to promoter hypomethylation was reported in PCa [83, 84]. Furthermore, aberrant histone methylation is found in PCa patients. Chervona et al., found reduced levels of H3K4me3 and H3K18Ac in PCa, which were associated with relapse and negative prognosis [85].

Fusion Gene in Racial Prostate Cancer Disparity

Gene rearrangement involving the androgen-regulated gene transmembrane protease serine 2 (*TMPRSS2*) and erythroblastosis virus E26 oncogene homolog (*ERG*) is the most common fusion gene in PCa. Its presence is found in approximately 50% of the patients diagnosed with PCa. However, this aberration is more frequently found in CA than in AA men, whose frequency is 31% [86]. Although ERG alteration is more commonly found in CA patients, AA patients with no ERG alteration exhibit higher-grade index tumors [87]. *TMPRSS2-ERG* fusion gene is associated with an aggressive tumor and is seen to be generated by gamma-irradiation-induced DNA double-strand breaks [88]. In addition, aberrant androgen receptor signaling may induce chromosome aberration.

Immune System in Prostate Cancer Disparity

The tumor microenvironment is constituted by various soluble factors such as cytokines, interleukins, proteins, several immune cells such as natural killer (NK), lymphocytes, macrophages, and non-immune cells such as fibroblast and endothelial cells. The fact that AA men develop more frequently PCa, and more aggressive diseases compared with CA men suggests that an inappropriate

tumor microenvironment may contribute to the increased disparity. A study conducted by Eastham et al., found that AA specimens exhibit higher inflammation compared with CA specimens in prostate biopsy specimens obtained from patients diagnosed with PCa [89]. In another study, Wallace et al., using microarray technology, evaluated the gene expression profile in PCa primary tumors obtained from a cohort of 69 patients (AA=33 and CA=36). They found that autocrine mobility factor receptor (AMFR), chemokine receptor 4 (CXCR4), and matrix metalloprotease 9 (MMP9) were the most differentially expressed genes [90]. In 2014, Kinseth et al., in a study integrated by 17 pairs of arrays for AA and CA, found a significant difference in the gene expression between both populations. Interestingly, most genes differentially expressed were associated with tumor-adjacent stroma, not tumor tissue [91]. Among the genes differentially expressed and associated with tumor tissue, genes involved in immune-related pathways were overexpressed [91], while from the genes differentially expressed in PCa stroma tissue, approximately 20% of them were involved in immune response, including cytokines such as TGF-β and IL-10 [91]. Interestingly, these cytokines are involved in immune suppression and PCa progression.

Another protein that seems to be involved in immune racial disparity is the well-known transmembrane protein MHC class I polypeptide-related sequence A (MICA). This protein participates in the surveillance and antitumor immunity by interacting with NK cells, cytotoxic T, and other T cell subsets expressing NKG2D receptor [92, 93]. Even though the expression of MICA allows immune cells to recognize tumors, some tumor cells exhibit an evasion mechanism by which MICA is cleaved from the membrane of the cancer. This soluble form (sMICA) binds the NKGD2 receptor, which is internalized. Thus, sMICA impairs the activation of immune cells [94, 95]. In 2004, Wu et al., reported a positive correlation between the level of sMICA and deficiency in NK function in patients with advanced PCa. Moreover, the group proposes sMICA as a novel biomarker for prostate cancer [96]. Recently, Sakiyama et al., in a cohort composed of a total of 52 patients diagnosed with PCa, including AA and CA men, found that prostate tumor tissues express a higher level of MICA compared with normal tissues. Furthermore, the MICA expression at molecular and protein levels was lower in AA patients compared with CA, and low levels of MICA were associated with poor prognosis [97]. Interestingly, sMICA was found in prostate cancer cell lines representative of CA but not in cell lines representative of AA. Thus, MICA expression participates in racial disparity. Another entity suggested to participate in immune race disparity in PCa is benign ethnic neutropenia, which is very frequent in AA [98, 99]. In 2012, Sadeghi et al., reported that neutropenia is an independent risk factor for developing poorly differentiated PCa among AA men [100]. However, more studies need to be performed to confirm the strength of this association.

Conclusion

Several factors are involved in the racial disparities observed between AA and CA men. Some increase the susceptibility to developing PCa, and others are related to aggressiveness and capacity to induce metastasis, resulting in the worst outcome. Among these factors, we can find mutations and gene variations such as polymorphisms, alteration of miRNA expression, aberrant activation of signaling pathways, epigenetic changes, and altered protein expression. Although for therapy use or the development of new ones, it is essential to know the molecular mechanisms implicated in the pathophysiology of PCa, some fundamental limitations still exist in the diagnosis and successful treatment. Due to the molecular complexity of PCa and the difficulties of therapies in targeting genetic factors such as mutations or polymorphisms, primary therapies are focused on surgical removal of the prostate combined with radiotherapy or chemotherapy to limit cancer cell proliferation. However, one of the best approaches that lead to successful therapies for cancer in general is preventive medicine since this allows for early diagnosis.

Preventive medicine encompasses educational strategies to draw attention to risk factors such as ancestry-related predisposition and environment. Recently, Garraway IP et al., [101] published a guideline for early screening to detect PCa in AA men, containing key points such as screening for blood PSA in the early 40s and family history. Furthermore, other strategies in preventive medicine include education related to dietary habits, smoking, and exposure to environmental pollutants. In conclusion, the combination of managing non-biological and biological factors involved in PCa is essential to eliminate racial disparities in diagnosis and treatment in AA men.

No Conflict Statement

All authors have participated in writing and have approved this version. The authors declare no potential conflicts of interest.

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