International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 621-631 www.ijprajournal.com ISSN: 2456-4494

A review on Prostate Cancer

Gyanendra Krishna Pandey[1], Anurag[1]*
[1]*Depertment of Pharmacy Practice, MM College of Pharmacy, Maharishi Markandeshwar (Deemed to be university), Mullana - 133207, Ambala, Haryana, India*

Date of Submission: 01-05-2024 Date of Acceptance: 10-05-2024

ABSTRACT
One of the diseases that affects males and has a major impact on the rising worldwide death rates for men is prostate cancer. Individuals with prostate cancer may have a localised or advanced stage of the illness at diagnosis. Our goal in writing this review is to present a comprehensive picture of prostate cancer, covering diagnosis, pathogenesis, progression, and available treatments. Prostate biopsies, digital rectal examinations, and prostate-specific antigen analyses are methods used to diagnose prostate cancer. The beginning, development, and spread of cancer are all associated with mutations in certain genes. Ablative radiation treatment, radical prostatectomy, and active surveillance are all used to treat localised prostate cancer. Chemotherapy, salvage radiation, and androgen deprivation treatment (ADT) are given to men with metastatic prostate cancer or those who have relapsed. Even with these choices, prostate cancer is still incurable. Currently, existing treatment methods work better when taken in tandem with one another. Research into alternative treatment modalities, including gene therapy, traditional medicine, and the use of nanotechnologies, is still ongoing in an effort to combat prostate cancer, drug resistance, and side effects associated with existing treatment options. This page provides an overview of the genes linked to prostate cancer, the treatments that are now accessible, and the state of research on complementary therapies.

Keywords : Prostate cancer, prostate cancer diagnosis, genetics of prostate cancer, prostate-specific antigen (PSA)

I. INTRODUCTION

Middle-aged men between the ages of 45 and 60 are most commonly affected by prostate cancer, which is the leading cause of cancer-related deaths in Western nations [1]. Prostate biopsy and analysis, PSA testing, digital rectal examination, magnetic resonance imaging (MRI), or health screening are among the methods used to identify prostate cancer in many men. Prostate cancer risk factors include age, weight, race, family history, and other environmental variables. Geographically and genetically, prostate cancer is a varied illness. There are variations in the prostate cancer epidemiology of various nations as a consequence of the interaction between genetics, environmental factors, and societal influences, which lowers estimates of the prostate cancer survival rate unique to a certain race [2]. Prostate cancer has a hereditary component, according to established research. Years of research have been dedicated to studying hereditary prostate cancer and the genetic component propensity to prostate cancer. Family inheritance is one of the strongest genetic risk factors for prostate cancer. The significance of hereditary prostate cancer has been demonstrated by twin studies as well as epidemiological research [3]. Numerous investigators have examined the potential contribution of genetic diversity to androgen production, metabolism, and function [4,5]. Chromosome rearrangements are among the molecular mechanisms that genomics research has linked to the development of some cancers [2]. Gene mutations are often a common cause of cancer. The genes involved in the androgen pathway and testosterone metabolism are candidate genes for the propensity to prostate cancer. The androgen receptor signalling pathway and testosterone are essential for the growth of prostatic epithelium and prostate cancer cells [6]. Prostate cancer can be treated specifically by identifying cancer biomarkers and focusing on certain genetic abnormalities. DNA tumour biomarkers, DNA biomarkers, and general biomarkers are among the biomarkers that can be employed for targeted therapy [7]. Androgen sensitivity and androgen insensitivity in prostate cancer refer to the degree of testosterone stimulation and the potential therapeutic options [8]. Active surveillance, chemotherapy, radiation therapy, hormone therapy, surgery, and cryotherapy are among the various treatment options for prostate cancer. The kind of tumour, PSA level, grade and stage, and potential

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 621-631 www.ijprajournal.com ISSN: 2456-4494

for recurrence all influence the treatment choices that are given to patients. For the treatment of low-risk prostate cancer, for instance, radiation therapy is combined with radical prostatectomy, a surgical approach that entails the removal of the prostate and adjacent tissues [9]. Hormonal therapy, commonly known as androgen-deprivation therapy, is advised for the treatment of malignancies that have returned and spread outside the prostate [1]. Severe side effects, including toxicity and lowered white and red blood cell counts, are linked to every treatment. These might result in tiredness, hair loss, peripheral neuropathy, erectile dysfunction and incontinence, metastasis, and finally, the development of resistance to the original treatment. The treatments that are now available are costly and have serious negative effects. It is essential to find new, more affordable chemotherapeutic drugs with little to no side effects and increased effectiveness [3]. In this study, we give a comprehensive overview of prostate cancer, including diagnosis, treatment choices, genetics and mutations that contribute to the disease's genesis and progression, and alternate therapy alternatives.

Epidemiology

One of the most prevalent cancers in males globally is prostate cancer [10]. According to GLOBOCAN, there were around 1,276,106 new instances of prostate cancer globally in 2018, accounting for 358,989 deaths; the disease is more common in industrialised nations. Globally, there are around 80,000 deaths from prostate cancer each year, and there is an average of 190,000 new cases each year [11]. Prostate cancer incidence varies globally among different geographic locations and ethnic groupings. In the globe, black males have the highest documented incidence rates of prostate cancer [12]. In America, Black Americans have incidence rates that are almost 60% greater than those of White men. The industrialised world's greatest incidence rates of prostate cancer are found in places where PSA testing is a common screening method and prostate cancer awareness is high [13]. According to the GLOBOCAN PSA test findings from 2012, there were significant incidence rates in the USA (97.2 per 100,000) and Australasia (111.6 per 100,000) [14]. Due to the world's population growth, which is expected to continue exponentially, and the enormous number of men who will be 65 years of age and older, prostate cancer is expected to climb to nearly 1.7 million new cases and 499,000 deaths worldwide by the year 2030 [15,16].

Diagnosis

The primary causes of the elevated death rate are therapy failure and prostate cancer diagnoses made at advanced stages of the illness. Prostate cancer cannot be identified by a single test; however, a digital rectal examination (DRE), in which the patient's rectum is probed with a gloved finger to measure the prostate gland's size and look for anomalies, is the standard method of diagnosis. The cornerstone for prostate cancer screening is still the prostate-specific antigen (PSA) test, but [17]. PSA is a glycoprotein released by the prostate gland's epithelial cells. Although it may also be detected in the bloodstream, it is typically present in semen [18]. Blood samples are obtained for PSA testing in order to determine the PSA level. The blood samples are then examined at a 4 ng/mL PSA cut-off point. PSA values more than 4 ng/mL indicate the necessity for further testing for the patient [19]. An estimated one in four patients with PSA values between 4 and 10 ng/mL may develop prostate cancer. Prostate cancer is more likely to occur in men whose PSA is higher than 10 ng/mL [20]. Prostate-specific antigen levels can therefore indicate benign pathologies like benign prostatic hyperplasia (BPH) and prostatitis rather than prostate cancer because PSA is specific to the prostate gland and not the cancer. Men without prostate cancer have also been reported to have elevated PSA levels. To determine whether cancer is present, a prostate tissue biopsy is often carried out [21].

During a biopsy, tiny tissue samples from the prostate gland are taken using a thin, hollow needle so they can be examined under a microscope. The biopsy can be carried out through the rectal wall (referred to as a transrectal biopsy) or through the skin between the anus and scrotum [22]. Transrectal ultrasonography (TRUS) and magnetic resonance imaging (MRI) are commonly used to detect the prostate gland during a biopsy. A powerful magnetic field and radio waves are used by an MRI scanner to provide detailed pictures of bodily tissue [23]. During a biopsy, aberrant regions of the prostate gland can be carefully targeted based on positive results from an MRI [24]. If a DRE, PSA test, and MRI were all negative, a multiparametric MRI may also be used as a triage test in place of a biopsy. A little probe called a TRUS is inserted into a patient's rectum. After the probe detects and interprets the echoes, a

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 621-631 www.ijprajournal.com ISSN: 2456-4494

computer programme converts them into a black-and-white picture of the organ [25]. However, recent advancements in machine learning algorithms and artificial intelligence (AI) have led to new classifications for prostate cancer. The paradigm of prostate cancer screening, diagnosis, and treatment has changed in recent years due to the availability of novel molecular markers and the introduction of sophisticated imaging techniques like prostate-specific membrane antigen positron emission tomography (PSMA-PET) scans and multiparametric magnetic resonance imaging (mpMRI) [27]. The most recent guidelines say that every male who is at risk of prostate cancer should first get a prostate MRI in order to prepare for a prostate biopsy [28,29].

Prostate cancer in the relationship with genetics

Prostate cancer is primarily associated with close familial lineage. Compared to males without a family history of prostate cancer, those with close relatives who have been diagnosed with the disease have a 50% higher chance of acquiring cancer [26]. Prostate cancer with an early beginning is typically found in first-degree relatives who have had prostate cancer detected in subsequent generations [31]. Studies using epidemiologic methods have demonstrated that genes predisposing to prostate cancer are inherited. According to case-control, twin, and family study analyses, there may be heritable components that contribute to the risk of prostate cancer. Certain gene mutations have been linked to hereditary prostate cancer, and people who carry these mutations are at higher risk of developing the illness, according to research [4]. Scientists employ multigene sequencing of males with prostate cancer diagnoses as well as those at high risk of getting cancer to evaluate inheritance patterns genetically. Significant mutations in DNA repair genes, including ATM, BRCA1, and BRCA2, were found in about 5.5% of these individuals. Due to specific genetic alterations that make African males more susceptible to prostate cancer, racial factors as well as environmental variables including migration and dietary habits are thought to have a role [21].

Single nucleotide polymorphisms (SNPs), somatic copy number alterations (SCNAs), and point mutations are examples of mutations that affect the DNA sequence and cause cancer [31]. Tumour suppressor genes can be turned off and oncogenes can be turned on by mutations, which can lead to prostate cell cancer [32]. This frequently results in unchecked cell division. Gene mutations can be acquired by an individual or handed down from one generation to the next. In the nucleus, acquired mutations often happen during DNA replication [33]. Prostate cancer biomarkers that are often utilised include the ATM gene, RNase L (HPC1, lq22), HOX genes, BRCA genes, MSR1 (8p), and ELAC2/HPC2 (17p11). The benefits of using biomarkers for diagnostic processes, staging, determining the disease's aggressiveness, and monitoring the therapy process are evident. Profiling technologies have led to several advancements, including as precision medicine and the discovery of new biomarkers that aid in diagnosis. Prostate health index (PHI), TMPRSS2-ERG fusion gene, 4K tests, and PCA3 are examples of contemporary biological markers that have been shown to improve PSA specificity and sensitivity, saving patients from undergoing biopsies and minimising overdiagnosis [76].

Treatment options

An additional approach to finding a gene-specific prostate cancer therapy for those individuals with advanced disease is the rapidly developing field of precision medicine. In order to identify diagnoses, prognostic therapies for patients, and precise dosage, it makes use of both genetic and environmental biomarkers. In order to identify patients with tumours displaying actionable targets and to facilitate more informed and precise treatment decisions, precision medicine uses genome sequencing to classify disorders [81].

Gene mutations linked to prostate cancer Men with mCRPC who have BRCA1 and BRCA2 are eligible for treatment with rucaparib or olaparib, as well as additional prostate cancer genes such as ATM, CDK12, CHECK2, CHECK1, PALB2, PP2R2A, and RAD54L that have shown positive response to olaparib therapy [82]. In a study of 1302 individuals with 67 BRCA mutation carriers, the impact of BRCA mutations on treatment results was examined. According to the findings, individuals who underwent radiation therapy or prostatectomy experienced metastases and had a worse chance of surviving when compared to those without BRCA gene abnormalities.

The BRCA1 gene was also shown to be 12% more prevalent in this research than the BRCA2 gene, which was just 2% common. A Chinese patient treated for prostate cancer with radiation and ADT was found to have the BRCA gene mutation (c.4211C > G) in a 2019 research. According to the study, individuals with this

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 621-631 www.ijprajournal.com ISSN: 2456-4494

particular mutation in prostate cancer responded well to both radiation and ADT, increasing the efficacy of the treatment [83]. The F876L mutation alters the binding ligand pocket in the AR, making it challenging to treat or build an effective CRPC. In a similar vein, the mutation W741L/C promotes particular AR binding that permits AR to transition into its active state. These mutations make it difficult to develop a successful treatment plan [84].

Clinical Management Procedures

When deciding on a course of therapy for prostate cancer, variables including age, comorbidities, and baseline urine function have all been taken into account in addition to the prognostic indicators, which include initial PSA level, clinical TNM stage, and Gleason's score [85]. The ability of doctors to categorise patients by risk and recommend therapy based on cancer prognosis and patient preference has improved due to advancements in the detection and treatment of prostate cancer [86]. For individuals with stage I–III prostate cancer, surveillance, prostatectomy, and radiation therapy are accepted as the conventional therapies.

All patients in stages IV and high-risk stages III can experience a long-lasting remission following androgen ablation by surgical or pharmaceutical castration. First-generation antiandrogens like flutamide and bicalutamide can help in this situation. However, the prognosis is dismal in stage IV due to the inevitability of castration resistance, which is characterised by genetic alterations in the androgen receptor [87].

II. CONCLUSIONS

Subsequent to lung illness, prostate cancer ranks among the world's primary causes of mortality for males. As indicators of the disease that reveal the stage and aetiology of the cancer, frequently altered genes, proteins, and pathways linked to an elevated risk of prostate cancer growth can be employed as biomarkers. Specifics about the kind of cancer treatment needed can also be determined by biomarkers. For prostate cancer, there is an immediate need for an efficient, tailored treatment. The majority of patients' quality of life is inevitably impacted by the various side effects of the prostate cancer therapies now in use, which only help a small number of people. Drug resistance is one of the negative side effects of chemotherapy, radiation therapy, and hormonal treatment, which continues to be a barrier to anticancer treatment. Numerous therapeutic plants, gene therapy, and the current study using nanotechnology have demonstrated the ability to lessen side effects and restore chemosensitivity in tumour cells that have become resistant to chemotherapy. Potential therapy options for prostate cancer include targeted medicines based on cellular pathways, genetic material encased in target-specific nanocarriers with controlled release, and medicinal plant fractions and chemicals.

REFERENCES

[1]. Chen J., Zhang D., Yan W., Yang D., Shen B. Translational Bioinformatics for Diagnostic and Prognostic Prediction of Prostate Cancer in the Next-Generation Sequencing Era. BioMed Res. Int. 2013;2013:901578. doi: 10.1155/2013/901578. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[2]. Hjelmborg J.B., Scheike T., Holst K., Skytthe A., Penney K.L., Graff R.E., Pukkala E., Christensen K., Adami H.-O., Holm N.V., et al. The Heritability of Prostate Cancer in the Nordic Twin Study of Cancer. Cancer Epidemiol. Biomark. Prev. 2014;23:2303–2310. doi: 10.1158/1055-9965.EPI-13-0568. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[3]. Termini D., Hartogh D.J.D., Jaglanian A., Tsiani E. Curcumin against Prostate Cancer: Current Evidence. Biomolecules. 2020;10:1536. doi: 10.3390/biom10111536. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[4]. Wen S., Chang H.-C., Tian J., Shang Z., Niu Y., Chang C. Stromal Androgen Receptor Roles in the Development of Normal Prostate, Benign Prostate Hyperplasia, and Prostate Cancer. Am. J. Pathol. 2015;185:293–301. doi: 10.1016/j.ajpath.2014.10.012. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[5]. Cittadini A., Isidori A.M., Salzano A. Testosterone therapy and cardiovascular diseases. Cardiovasc. Res. 2021;118:2039–2057. doi: 10.1093/cvr/cvab241. [PubMed] [CrossRef] [Google Scholar]

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 621-631 www.ijprajournal.com ISSN: 2456-4494

[6]. Bluemn E.G., Nelson P.S. The androgen/androgen receptor axis in prostate cancer. Curr. Opin. Oncol. 2012;24:251–257. doi: 10.1097/CCO.0b013e32835105b3. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[7]. Ziaran S., Novakova Z.V., Böhmer D., Danišovič L. Biomarkers for determination prostate cancer: Implication for diagnosis and prognosis. Neoplasma. 2015;62:683–691. doi: 10.4149/neo_2015_082. [PubMed] [CrossRef] [Google Scholar]

[8]. Takayama K.-I. Splicing Factors Have an Essential Role in Prostate Cancer Progression and Androgen Receptor Signaling. Biomolecules. 2019;9:131. doi: 10.3390/biom9040131. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[9]. Bach C., Pisipati S., Daneshwar D., Wright M., Rowe E., Gillatt D., Persad R., Koupparis A. The status of surgery in the management of high-risk prostate cancer. Nat. Rev. Urol. 2014;11:342–351. doi: 10.1038/nrurol.2014.100. [PubMed] [CrossRef] [Google Scholar]

[10]. Ziegler A., Koch A., Krockenberger K., Großhennig A. Personalized medicine using DNA biomarkers: A review. Qual. Life Res. 2012;131:1627–1638. doi: 10.1007/s00439-012-1188-9. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[11]. Rawla P. Epidemiology of Prostate Cancer. World J. Oncol. 2019;10:63–89. doi: 10.14740/wjon1191. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[12]. Barbieri C., Bangma C.H., Bjartell A., Catto J., Culig Z., Grönberg H., Luo J., Visakorpi T., Rubin M. The Mutational Landscape of Prostate Cancer. Eur. Urol. 2013;64:567–576. doi: 10.1016/j.eururo.2013.05.029. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[13]. Haas G.P., Delongchamps N., Brawley O.W., Wang C.Y., De La Roza G. The worldwide epidemiology of prostate cancer: Perspectives from autopsy studies. Can. J. Urol. 2008;15:3866–3871. [PMC free article] [PubMed] [Google Scholar]

[14]. Sung H., Ferlay J., Siegel R.L., Laversanne M., Soerjomataram I., Jemal A., Bray F. Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. CA Cancer J. Clin. 2021;71:209–249. doi: 10.3322/caac.21660. [PubMed] [CrossRef] [Google Scholar]

[15]. Taitt H.E. Global Trends and Prostate Cancer: A Review of Incidence, Detection, and Mortality as Influenced by Race, Ethnicity, and Geographic Location. Am. J. Men's Health. 2018;12:1807–1823. doi: 10.1177/1557988318798279. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[16]. Bashir M.N. Epidemiology of Prostate Cancer. Asian Pac. J. Cancer Prev. 2015;16:5137–5141. doi: 10.7314/APJCP.2015.16.13.5137. [PubMed] [CrossRef] [Google Scholar]

[17]. Ferlay J., Parkin D., Steliarova-Foucher E. Estimates of cancer incidence and mortality in Europe in 2008. Eur. J. Cancer. 2010;46:765–781. doi: 10.1016/j.ejca.2009.12.014. [PubMed] [CrossRef] [Google Scholar]

[18]. Matshela R.F., Maree L., van Belkum C. Prevention and Detection of Prostate Cancer. Cancer Nurs. 2014;37:189–197. doi: 10.1097/NCC.0b013e31829194d2. [PubMed] [CrossRef] [Google Scholar]

[19]. Babb C., Urban M., Kielkowski D., Kellett P. Prostate Cancer in South Africa: Pathology Based National Cancer Registry Data (1986–2006) and Mortality Rates (1997–2009) Prostate Cancer. 2014;2014:419801. doi: 10.1155/2014/419801. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[20]. Altwaijry N., Somani S., Parkinson J., Tate R., Keating P., Warzecha M., MacKenzie G.R., Leung H.Y., Dufès C. Regression of prostate tumors after intravenous administration of lactoferrin-bearing polypropylenimine dendriplexes encoding TNF-α, TRAIL, and interleukin-12. Drug Deliv. 2018;25:679–689. doi: 10.1080/10717544.2018.1440666. [P

MC free article] [PubMed] [CrossRef] [Google Scholar]

[21]. Adhyam M., Gupta A.K. A Review on the Clinical Utility of PSA in Cancer Prostate. Indian J. Surg. Oncol. 2012;3:120–129. doi: 10.1007/s13193-012-0142-6. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[22]. Suzuki K., Kise H., Nishioka J., Hayashi T. The Interaction among Protein C Inhibitor, Prostate-Specific Antigen, and the Semenogelin System. Semin. Thromb. Hemost. 2007;33:46–52. doi: 10.1055/s-2006-958461. [PubMed] [CrossRef] [Google Scholar]

[23]. Lamy P.-J., Allory Y., Gauchez A.-S., Asselain B., Beuzeboc P., de Cremoux P., Fontugne J., Georges A., Hennequin C., Lehmann-Che J., et al. Prognostic Biomarkers Used for Localised Prostate Cancer Management: A Systematic Review. Eur. Urol. Focus. 2018;4:790–803. doi: 10.1016/j.euf.2017.02.017. [PubMed] [CrossRef] [Google Scholar]

[24]. Meyer A.R., Joice G.A., Schwen Z.R., Partin A.W., Allaf M.E., Gorin M.A. Initial Experience Performing In-office Ultrasound-guided Transperineal Prostate Biopsy Under Local Anesthesia Using the PrecisionPoint Transperineal Access System. Urology. 2018;115:8–13. doi: 10.1016/j.urology.2018.01.021. [PubMed] [CrossRef] [Google Scholar]

[25]. Niraj L.K. MRI in Dentistry—A Future Towards Radiation Free Imaging—Systematic Review. J. Clin. Diagn. Res. 2016;10:ZE14–ZE19. doi: 10.7860/JCDR/2016/19435.8658. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[26]. Chopra S., Foltz W.D., Milosevic M.F., Toi A., Bristow R.G., Ménard C., Haider M.A. Comparing oxygen-sensitive MRI (BOLD R2*) with oxygen electrode measurements: A pilot study in men with prostate cancer. Int. J. Radiat. Biol. 2009;85:805–813. doi: 10.1080/09553000903043059. [PubMed] [CrossRef] [Google Scholar]

[27]. Kasivisvanathan V., Rannikko A.S., Borghi M., Panebianco V., Mynderse L.A., Vaarala M.H., Briganti A., Budäus L., Hellawell G., Hindley R.G., et al. MRI-Targeted or Standard Biopsy for Prostate-Cancer Diagnosis. N. Engl. J. Med. 2018;378:1767–1777. doi: 10.1056/NEJMoa1801993. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[28]. Albright F., Stephenson R.A., Agarwal N., Teerlink C.C., Lowrance W.T., Farnham J.M., Albright L.A.C. Prostate cancer risk prediction based on complete prostate cancer family history. Prostate. 2015;75:390–398. doi: 10.1002/pros.22925. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[29]. Prando A. Diffusion-weighted MRI of peripheral zone prostate cancer: Comparison of tumor apparent diffusion coefficient with Gleason score and percentage of tumor on core biopsy. Int. Braz. J. Urol. 2010;36:504–517. doi: 10.1590/S1677-55382010000400018. [PubMed] [CrossRef] [Google Scholar]

[30]. Manish Kumar Maity, Mamta Naagar, "Autoimmune Neurogenic Dysphagia", International Journal of Science and Research (IJSR), Volume 11 Issue 7, July 2022, pp. 447-463, https://www.ijsr.net/getabstract.php?paperid=SR22630151732.

[31]. Manish Kumar Maity, Mamta Naagar, "A Review on Headache: Epidemiology, Pathophysiology, Classifications, Diagnosis, Clinical Management and Treatment Modalities", International Journal of Science and Research (IJSR), Volume 11 Issue 7, July 2022, pp. 506-515, https://www.ijsr.net/getabstract.php?paperid=SR22703111804.

[32]. Md Shamshir Alam , Manish Kumar Maity , Abdul Salam Nazmi , Md Sarfaraz Alam , Md Salahuddin Ansari. Oral Health Issues And Preventive Measures In Geriatric Populations. Journal of Pharmaceutical Negative Results [Internet]. 2022 Dec. 31 [cited 2023 Jun. 24];:2647-55. Available from: https://www.pnrjournal.com/index.php/home/article/view/9175

[33]. Nikita Sharma , Md Shamshir Alam , Anubha Sharma , Sanyam Garg , Manish Kumar Maity. Colorectal Cancer In Young Adults: Epidemiology, Risk Factors, Development, Symptoms, Traditional Herbal Therapy And Prevention. Journal of Pharmaceutical Negative Results [Internet]. 2022 Dec. 31 [cited 2023 Jun. 24];:1370-82. Available from: https://pnrjournal.com/index.php/home/article/view/6991

[34]. Ehteshamul Haque , Faiz Ahmed , Priyanka Chaurasiya , Neha Yadav , Nikita Dhiman , Manish Kumar Maity. A REVIEW ON ANTIDEPRESSANT EFFECT OF HERBAL DRUGS. Journal of Pharmaceutical Negative Results [Internet]. 2023 Feb. 17 [cited 2023 Jun. 24];:2716-23. Available from: https://www.pnrjournal.com/index.php/home/article/view/8841

[35]. OmveerSingh, Shailesh Sharma, Mamta Naagar, Manish Kumar Maity, Eletriptan As Treatment Option For Acute Migraine, International Journal Of Innovations & Research Analysis (Ijira),02, 03(II), September, 2022, Pp 15-24.

[36]. Priyanka Tanwar, Mamta Naagar, and Manish Kumar Maity, "Relationship between Type 2 Diabetes Mellitus and Osteoarthritis,"International Research Journal of Pharmacy and Medical Sciences (IRJPMS), Volume 6, Issue 2, pp. 59-70, 2023 (PDF) Relationship between Type 2 Diabetes Mellitus and Osteoarthritis. Available from: https://www.researchgate.net/publication/369022995_Relationship_between_Type_2_Diabetes_Mellitus_and_Osteoarthritis [accessed Jun 23 2023].

[37]. Omveer Singh, Shailesh Sharma, Mamta Naagar, Manish Kumar Maity, Oral And Parenteral To Minimize The Nasal Delivery By Thermoreversible Mucoadhesive –A Review, International Journal Of Creative Research Thoughts (Ijcrt), 09/2022,10(9) Pp.-356-371.

[38]. Md Shamshir Alam, Garima Malik, Priyanka Tanwar, Mamta Naagar, Tarun Singh, Omveer Singh, Manish Kumar Maity, A Review on Small-Cell Lung Cancer: Epidemiology, Pathophysiology, RiskFactors, Diagnosis, Clinical Management and Treatment Modalities, International Journal of Current Science Research and Review (ijcsrr), 06(01): 129-151.

[39]. Priyanka Tanwar, Mamta Naagar, and Manish Kumar Maity, "Relationship between Diabetes Mellitus and Bone Health – A Review,"International Research Journal of Pharmacy and Medical Sciences (IRJPMS), Volume 6, Issue 2, pp. 46-58, 2023. (PDF) Relationship between Diabetes Mellitus and Bone Health - A Review. Available from: https://www.researchgate.net/publication/369022910_Relationship_between_Diabetes_Mellitus_and_Bone_Health_-_A_Review [accessed Jun 23 2023].

[40]. Manish Kumar Maity. A review on Helicobacter pylori Infection. ijmsdr [Internet]. 2022Sep.17 [cited 2023Jun.23];6(9). Available from: https://www.ijmsdr.com/index.php/ijmsdr/article/view/950

[41]. Md Shamshir Alam , Manish Kumar Maity , Abdul Salam Nazmi , Md Sarfaraz Alam , Md Salahuddin Ansari (2022) "Oral Health Issues And Preventive Measures In Geriatric Populations",Journal of Pharmaceutical Negative Results, pp. 2647–2655. doi: 10.47750/pnr.2022.13.S10.316.

[42]. Marlin R., Créoff M., Merle S., Jean-Marie-Flore M., Rose M., Malsa S., Promeyrat X., Martin F., Comlan G., Rabia N., et al. Mutation HOXB13 c.853delT in Martinican prostate cancer patients. Prostate. 2020;80:463–470. doi: 10.1002/pros.23960. [PubMed] [CrossRef] [Google Scholar]

[43]. Manzari Z., Mehrabani-Yeganeh H., Nejati-Javaremi A., Moradi M.H., Gholizadeh M. Detecting selection signatures in three Iranian sheep breeds. Anim. Genet. 2019;50:298–302. doi: 10.1111/age.12772. [PubMed] [CrossRef] [Google Scholar]

[44]. Jeong T.-O., Oh K.-J., Nguyen N.T.X., Kim Y.-R., Kim M.S., Lee S.D., Ryu S.B., Jung C. Evaluation of HOXB13 as a molecular marker of recurrent prostate

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 621-631 www.ijprajournal.com ISSN: 2456-4494

cancer. Mol. Med. Rep. 2012;5:901–904. doi: 10.3892/mmr.2012.769. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[45]. Guarini A., Marinelli M., Tavolaro S., Bellacchio E., Magliozzi M., Chiaretti S., De Propris M.S., Peragine N., Santangelo S., Paoloni F., et al. ATM gene alterations in chronic lymphocytic leukemia patients induce a distinct gene expression profile and predict disease progression. Haematologica. 2012;97:47–55. doi: 10.3324/haematol.2011.049270. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[46]. Antonarakis E.S., Lu C., Wang H., Luber B., Nakazawa M., Roeser J.C., Chen Y., Mohammad T.A., Chen Y., Fedor H.L., et al. AR-V7 and Resistance to Enzalutamide and Abiraterone in Prostate Cancer. N. Engl. J. Med. 2014;371:1028–1038. doi: 10.1056/NEJMoa1315815. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[47]. Gallagher D.J., Gaudet M.M., Pal P., Kirchhoff T., Balistreri L., Vora K., Bhatia J., Stadler Z., Fine S.W., Reuter V., et al. Germline BRCA Mutations Denote a Clinicopathologic Subset of Prostate Cancer. Clin. Cancer Res. 2010;16:2115–2121. doi: 10.1158/1078-0432.CCR-09-2871. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[48]. Xu B., Tong N., Li J.-M., Zhang Z.-D., Wu H.-F. ELAC2 polymorphisms and prostate cancer risk: A meta-analysis based on 18 case–control studies. Prostate Cancer Prostatic Dis. 2010;13:270–277. doi: 10.1038/pcan.2010.6. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[49]. Suzuki T., Li W., Zhang Q., Karim A., Novak E.K., Sviderskaya E.V., Hill S.P., Bennett D.C., Levin A.V., Nieuwenhuis H.K., et al. Hermansky-Pudlak syndrome is caused by mutations in HPS4, the human homolog of the mouse light-ear gene. Nat. Genet. 2002;30:321–324. doi: 10.1038/ng835. [PubMed] [CrossRef] [Google Scholar]

[50]. Moore K.J., Freeman M.W. Scavenger Receptors in Atherosclerosis. Arter. Thromb. Vasc. Biol. 2006;26:1702–1711. doi: 10.1161/01.ATV.0000229218.97976.43. [PubMed] [CrossRef] [Google Scholar]

[51]. Leighton X., Bera A., Eidelman O., Eklund M., Puthillathu N., Pollard H.B., Srivastava M. High ANXA7 Potentiates Eucalyptol Toxicity in Hormone-refractory Prostate Cancer. Anticancer Res. 2018;38:3831–3842. doi: 10.21873/anticanres.12667. [PubMed] [CrossRef] [Google Scholar]

[52]. Srivastava M., Leighton X., Starr J., Eidelman O., Pollard H.B. Diverse Effects of ANXA7 and p53 on LNCaP Prostate Cancer Cells Are Associated with Regulation of SGK1 Transcription and Phosphorylation of the SGK1 Target FOXO3A. BioMed Res. Int. 2014;2014:193635. doi: 10.1155/2014/193635. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[53]. Miura Y., Kataoka H., Joh T., Tada T., Asai K., Nakanishi M., Okada N., Okada H. Susceptibility to killer T cells of gastric cancer cells enhanced by mitomycin-C involves induction of ATBF1 and activation of p21 (Waf1/Cip1) promoter. Microbiol. Immunol. 2004;48:137–145. doi: 10.1111/j.1348-0421.2004.tb03491.x. [PubMed] [CrossRef] [Google Scholar]

[54]. Kai K., Zhang Z., Yamashita H., Yamamoto Y., Miura Y., Iwase H. Loss of heterozygosity at the ATBF1-A locus located in the 16q22 minimal region in breast cancer. BMC Cancer. 2008;8:262. doi: 10.1186/1471-2407-8-262. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[55]. Sun X., Frierson H.F., Chen C., Li C., Ran Q., Otto K.B., Cantarel B.M., Vessella R.L., Gao A.C., Petros J., et al. Frequent somatic mutations of the transcription factor ATBF1 in human prostate cancer. Nat. Genet. 2005;37:407–412. doi: 10.1038/ng1528. [PubMed] [CrossRef] [Google Scholar]

[56]. Chang B.-L., Zheng S.L., Isaacs S.D., Wiley K.E., Turner A., Li G., Walsh P.C., Meyers D.A., Isaacs W.B., Xu J. A Polymorphism in the CDKN1B Gene Is Associated with Increased Risk of

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 621-631 www.ijprajournal.com ISSN: 2456-4494

Hereditary Prostate Cancer. Cancer Res. 2004;64:1997–1999. doi: 10.1158/0008-5472.CAN-03-2340. [PubMed] [CrossRef] [Google Scholar]

[57]. Soyano A.E., Baldeo C., Kasi P.M. BRCA Mutation and Its Association With Colorectal Cancer. Clin. Color. Cancer. 2018;17:e647–e650. doi: 10.1016/j.clcc.2018.06.006. [PubMed] [CrossRef] [Google Scholar]

[58]. Sirma H., Broemel M., Stumm L., Tsourlakis T., Steurer S., Tennstedt P., Salomon G., Michl U., Haese A., Simon R., et al. Loss of CDKN1B/p27Kip1 expression is associated with ERG fusion-negative prostate cancer, but is unrelated to patient prognosis. Oncol. Lett. 2013;6:1245–1252. doi: 10.3892/ol.2013.1563. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[59]. Slavin D.A., Koritschoner N.P., Prieto C.C., López-Díaz F.J., Chatton B., Bocco J.L. A new role for the Krüppel-like transcription factor KLF6 as an inhibitor of c-Jun proto-oncoprotein function. Oncogene. 2004;23:8196–8205. doi: 10.1038/sj.onc.1208020. [PubMed] [CrossRef] [Google Scholar]

[60]. Narla G., DiFeo A., Fernandez Y., Dhanasekaran S.M., Huang F., Sangodkar J., Hod E., Leake D., Friedman S.L., Hall S.J., et al. KLF6-SV1 overexpression accelerates human and mouse prostate cancer progression and metastasis. J. Clin. Investig. 2008;118:2711–2721. doi: 10.1172/JCI34780. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[61]. Multiple Sclerosis. Cold Spring Harbor Perspectives in Medicine; Cold Spring Harbor (New York): Cold Spring Harbor Laboratory Press. $135.00. viii + 362 p.; ill.; index. ISBN: 9781621820765. 2018. [(accessed on 25 May 2022)];Q. Rev. Biol. 2019 94:450. doi: 10.1086/706427. Available online: https://www.journals.uchicago.edu/doi/10.1086/706427 [CrossRef] [Google Scholar]

[62]. Rebello R.J., Pearson R.B., Hannan R.D., Furic L. Therapeutic Approaches Targeting MYC-Driven Prostate Cancer. Genes. 2017;8:71. doi: 10.3390/genes8020071. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[63]. Chen H., Liu W., Roberts W., Hooker S., Fedor H., DeMarzo A., Isaacs W., Kittles R.A. 8q24 allelic imbalance and MYC gene copy number in primary prostate cancer. Prostate Cancer Prostatic Dis. 2010;13:238–243. doi: 10.1038/pcan.2010.20. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[64]. Gurel B., Ali T.Z., Montgomery E.A., Begum S., Hicks J., Goggins M., Eberhart C.G., Clark D.P., Bieberich C.J., Epstein J.I., et al. NKX3.1 as a Marker of Prostatic Origin in Metastatic Tumors. Am. J. Surg. Pathol. 2010;34:1097–1105. doi: 10.1097/PAS.0b013e3181e6cbf3. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[65]. Menini T., Gugliucci A. Paraoxonase 1 in neurological disorders. Redox Rep. 2014;19:49–58. doi: 10.1179/1351000213Y.0000000071. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[66]. Stevens V.L., Rodriguez C., Talbot J.T., Pavluck A.L., Thun M.J., Calle E.E. Paraoxonase 1 (PON1) polymorphisms and prostate cancer in the CPS-II Nutrition Cohort. Prostate. 2008;68:1336–1340. doi: 10.1002/pros.20796. [PubMed] [CrossRef] [Google Scholar]

[67]. Markowska A., Pawałowska M., Lubin J., Markowska J. Signalling pathways in endometrial cancer. Współczesna Onkol. 2014;18:143–148. doi: 10.5114/wo.2014.43154. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[68]. Steelman L.S., Chappell W.H., Abrams S.L., Kempf C.R., Long J., Laidler P., Mijatovic S., Maksimovic-Ivanic D., Stivala F., Mazzarino M.C., et al. Roles of the Raf/MEK/ERK and PI3K/PTEN/Akt/mTOR pathways in controlling growth and sensitivity to therapy-implications for cancer and aging. Aging. 2011;3:192–222. doi: 10.18632/aging.100296. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

International Journal of Pharmaceutical Research and Applications
Volume 9, Issue 3 May-June 2024, pp: 621-631 www.ijprajournal.com ISSN: 2456-4494

[69]. Fraser M., Zhao H., Luoto K.R., Lundin C., Coackley C., Chan N., Joshua A.M., Bismar T.A., Evans A., Helleday T., et al. PTEN Deletion in Prostate Cancer Cells Does Not Associate with Loss of RAD51 Function: Implications for Radiotherapy and Chemotherapy. Clin. Cancer Res. 2012;18:1015–1027. doi: 10.1158/1078-0432.CCR-11-2189. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[70]. Jamaspishvili T., Berman D.M., Ross A.E., Scher H.I., De Marzo A.M., Squire J.A., Lotan T.L. Clinical implications of PTEN loss in prostate cancer. Nat. Rev. Urol. 2018;15:222–234. doi: 10.1038/nrurol.2018.9. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[71]. Penta J.S., Johnson F., Wachsman J.T., Copeland W.C. Mitochondrial DNA in human malignancy. Mutat. Res. Mutat. Res. 2001;488:119–133. doi: 10.1016/S1383-5742(01)00053-9. [PubMed] [CrossRef] [Google Scholar]

[72]. Petros J.A., Baumann A.K., Ruiz-Pesini E., Amin M.B., Sun C.Q., Hall J., Lim S., Issa M.M., Flanders W.D., Hosseini S.H., et al. mtDNA mutations increase tumorigenicity in prostate cancer. Proc. Natl. Acad. Sci. USA. 2005;102:719–724. doi: 10.1073/pnas.0408894102. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[73]. Sanchez-Vega F., Mina M., Armenia J., Chatila W.K., Luna A., La K., Dimitriadoy S., Liu D.L., Kantheti H.S., Heins Z., et al. Abstract 3302: The molecular landscape of oncogenic signaling pathways in The Cancer Genome Atlas. Cancer Res. 2018;78:3302. doi: 10.1158/1538-7445.AM2018-3302. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[74]. Cox A.D., Der C.J. Ras history: The Saga Continues. Small GTPases. 2010;1:2–27. doi: 10.4161/sgtp.1.1.12178. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[75]. Hessels D., Schalken J.A. Urinary biomarkers for prostate cancer: A review. Asian J. Androl. 2013;15:333–339. doi: 10.1038/aja.2013.6. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[76]. Alford A.V., Brito J.M., Yadav K.K., Yadav S.S., Tewari A.K., Renzulli J. The Use of Biomarkers in Prostate Cancer Screening and Treatment. Rev. Urol. 2017;19:221–234. doi: 10.3909/riu0772. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[77]. Porzycki P., Ciszkowicz E. Modern biomarkers in prostate cancer diagnosis. Cent. Eur. J. Urol. 2020;73:300–306. doi: 10.5173/ceju.2020.0067r. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[78]. Shen M.M., Abate-Shen C. Molecular genetics of prostate cancer: New prospects for old challenges. Genes Dev. 2010;24:1967–2000. doi: 10.1101/gad.1965810. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[79]. Duan R., Du W., Guo W. EZH2: A novel target for cancer treatment. J. Hematol. Oncol. 2020;13:104. doi: 10.1186/s13045-020-00937-8. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[80]. Kipriyanov E.A., Karnaukh P.A., Vazhenin I.A., Vazhenin A.V. Radical prostatectomy and robotic radiosurgery as treatment options for localized prostate cancer. Sib. J. Oncol. 2020;19:50–56. doi: 10.21294/1814-4861-2020-19-1-50-56. [CrossRef] [Google Scholar]

[81]. Mateo L., Duran-Frigola M., Gris-Oliver A., Palafox M., Scaltriti M., Razavi P., Chandarlapaty S., Arribas J., Bellet M., Serra V., et al. Personalized cancer therapy prioritization based on driver alteration co-occurrence patterns. Genome Med. 2020;12:78. doi: 10.1186/s13073-020-00774-x. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[82]. Giri V.N., Morgan T.M., Morris D.S., Berchuck J.E., Hyatt C., Taplin M., Morris F.D.S., Ms C.C.H. Genetic testing in prostate cancer management: Considerations informing primary care. CA: A Cancer J. Clin. 2022;72:360–

371. doi: 10.3322/caac.21720. [PubMed] [CrossRef] [Google Scholar]

[83]. Liu Q., Tong D., Liu G., Yi Y., Xu J., Yang X., Wang L., Zhang J., Ye J., Zhang Y., et al. A novel BRCA2 mutation in prostate cancer sensitive to combined radiotherapy and androgen deprivation therapy. Cancer Biol. Ther. 2018;19:669–675. doi: 10.1080/15384047.2018.1451278. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[84]. McCrea E.M., Lee D.K., Sissung T.M., Figg W.D. Precision Medicine Applications in Prostate Cancer. Ther. Adv. Med. Oncol. 2018;10:175883591877692. doi: 10.1177/1758835918776920. [PMC free article] [PubMed] [CrossRef] [Google Scholar]

[85]. Trewartha D., Carter K. Advances in prostate cancer treatment. Nat. Rev. Drug Discov. 2013;12:823–824. doi: 10.1038/nrd4068. [PubMed] [CrossRef] [Google Scholar]

[86]. Dunn M.W., Kazer M.W. Prostate Cancer Overview. Semin. Oncol. Nurs. 2011;27:241–250. doi: 10.1016/j.soncn.2011.07.002. [PubMed] [CrossRef] [Google Scholar]

[87]. Lima Z.S., Ghadamzadeh M., Arashloo F.T., Amjad G., Ebadi M.R., Younesi L. Recent advances of therapeutic targets based on the molecular signature in breast cancer: Genetic mutations and implications for current treatment paradigms. J. Hematol. Oncol. 2019;12:39. doi: 10.1186/s13045-019-0725-6. [PMC free article] [PubMed] [CrossRef] [Google Scholar]