LUPINE PUBLISHERS

Open Access Journal of Oncology and Medicine

DOI: 10.32474/OAJOM.2021.05.000208

ISSN: 2638-5945

Review Article

Prostate Cell Lines

Abdulghani A Naeem[1], Saud A Abdulsamad[1], Asmaa Al Bayati[1], Jiacheng Zhang[1], Mohammed I Malki[2], Hongwen Ma[3], and Youqiang Ke[1]*

[1]*Department of Molecular & Clinical Cancer Medicine, Liverpool University, Liverpool, United Kingdom*

[2]*College of Medicine, QU Health, Qatar university, Doha, Qatar*

[3]*Department of Urology, Institute of Urology, West China Hospital, Sichuan University, China*

***Corresponding author:** Youqiang Ke, Professor, Department of Molecular & Clinical Cancer Medicine, Liverpool University, L69 3GA, United Kingdom

Received: February 11, 2022 **Published:** February 25, 2022

Abstract

When it comes to studying biological processes, cell lines are typically utilized in lieu of original cell samples. Like in the studies for other cancer types, researchers in prostate cancer can be constrained in their ability to discover new treatments because of a lack of cell lines to investigate pre-clinical status. There are various forms of prostate cancer cell lines that are reviewed in this work. A cautionary note is in need since cell lines may not always correctly mimic the original cells. Cancerous cells are immortal and using cell lines produced from cancer cells as a model to better understand cancer and to develop novel therapies are common in research. Apart from the prostate cancer cells, we also reviewed two cell lines PNT2 and RWPE-1 which were established from non-neoplastic male prostatic epithelial cells.

Introduction

Cancers are known for their ability to prolong life indefinitely [1,2]. However, it remains a mystery how mortal somatic cells become the source of immortal malignancies. Cancerous cells are immortal, despite the fact that healthy somatic cells may develop into organs as well as creatures that include much more cells than lethal tumors [3-11]. By exceeding the Hayflick threshold, which is approximately 50 cycles in vitro, immortality is established operationally. Telomerase stimulation is now the most widely accepted explanation of immortality [4-6]. Cancers are supposed to gain immortality via the stimulation of telomerase, which is a gene that is normally shut off throughout development in somatic cells. To put it another way, cells that have maintained their telomeres by the acts of telomerase process are considered to be immortalized. All individual tumors seem to be governed by the process of cell immortalization.

It is these cells that serve as a starting point for tumor development and are known as the cancer cells of origin. Unlike cancer stem cells, which constitute the cellular subfractions capable of regenerating tumors, these cells are classified in a different way. It's been a major focus of cancer research to identify the cells that give rise to the disease. Since there is so much interest in testing the concept that tumors are caused by various cell types, this has resulted in a lot of research being done in this area. This knowledge will aid in the early detection and precise prognosis of cancer, as well as in the development of new preventative treatments for people at high risk. Based on the histological appearance of malignancies, it was formerly considered that they had a cellular origin. We now know, based on our existing understanding, that tumor specimens may be deceiving when random as well as static observations are made. A direct genetic method should be used to test any hypotheses. Tumors may have gene expression patterns that are more like those of their own cells' ancestors than those of other cell types within the same tissue, which is a similar but much more elegant concept. The basal-like breast cancer may originate from luminal epithelial progenitors in the mammary gland luminal epithelium. Gene expression patterns may be used to classify brain tumors with similar histological characteristics into separate groups that represent the cellular genesis of the tumors. Molecular profiles don't always line up with tumor pathology, according to these findings. It is still necessary to do more direct genetic research in order to verify the findings drawn from these sorts of studies. Cell lines having diverse lineage features from human or mouse tissues may be established, transformed, and then analyzed

to see whether the resultant tumors have a distinctive pathological appearance. Using these cell lines, Ince et al. were able to generate mammary gland epithelial cells with a luminal and a myoepithelial phenotype. In the presence of the identical set of oncogenes, the two kinds of cells differentiated into tumors with unique phenotypic characteristics and propensity for malignancy.

When a multicellular organism's cells are mutated, they may continue to divide forever despite the fact that they would ordinarily stop proliferating at a certain point. This is known as an immortalized cell line. Because of this, the cells may be cultivated in vitro for lengthy periods of time. In a laboratory, cell lines are the simplest way to grow viruses. But primary cells taken from a live animal or person are the sole option for viral culture in the absence of cell lines that are sensitive to virus infection. Cells derived from in vitro altered cell lines or malignant cells may be cultivated in monolayer or suspended form, making them infinite cell lines [7]. There's a 12- to 14-hour growth period for these cells; they're capable of being grown forever. When doing scientific studies, it's usual to employ human cell lines. There has been a long history in which cell lines have served as the backbone of research into the mechanisms involved, the discovery of new drugs, and the application of results to human illness. Human cell lines are commonly used in the majority of labs [8]. Several were formed generations earlier and dispersed around the scientific community. A prevalent belief is that human cell lines produced in one laboratory are identical to those in another. Not at all! The molecular and cellular phenotype may change as a consequence of changes in the number of passages or the environment in which the cells are grown. A new Endocrine Society editorial guideline mandates that all cell lines employed and reported in freshly submitted and updated publications be authenticated in order to ensure uniformity. Comparability and reproducibility among researchers are made possible by the disclosure of information including where and then when the cells were collected, if as well as how they were examined and verified, and when the last test was performed. With a lifetime prevalence of one in six, men in the United States have the second most prevalent cause of cancer-related death from cancer (9-10). There are far more cell lines that could also tell us about the biological condition of the prostate and can be utilized to study the development of prostate cancer. This means that new prostate cell lines must be developed immediately to mimic human tissue samples in terms of the diverse phenotypes seen. Using tissue recombination in immunodeficient mice models to study the functional modification of real prostatic tissues is a significant tool [11]. As a result, most current research lacks a thorough knowledge of the pathways that lead to prostate cancer.

PNT-2 Cells

The human cell line PNT2 came from the prostate gland tissue of a dead 33-year-old man. A plasmid harboring a Simian virus genome with a faulty origin of replication (SV40 ori-) was employed to immortalize the cell line [12]. The Simian virus is routinely employed to memorialize mammalian epithelial cells. PNT2 cells have the SV40 genome and express big T protein. A well-differentiated shape and the expression of cytokeratin distinguish these cells from luminal cells of the prostate gland [13]. PNT2 cells are connected cell lines which develop with an epithelial appearance. PNT2 produces cytokeratin (CK), member of the keratin family. The keratin family are crucial in maintaining the architecture of epithelial cells. CK8 and CK18 are joined together as partners and operate as plasminogen receptors [13]. CK19 is produced in the periderm and is a characteristic of differentiated luminal cells.

PNT2 cells are often utilized in medical research, for instance by Baker et al in 2008, who employed secondary ion mass spectrometry to discriminate between prostate cancer cells and non-malignant cells [14]. They have also been employed by Faria, et al. in 2008 as part of an inquiry into the assessment of the elastic characteristics of prostate cancer utilizing Atomic Force Microscopy (AFM). Another example of PNT2's use is by Smith et al in 1998, when sodium channel expression was demonstrated to boost the intrusiveness of rat and human prostate cancer cells. The medium that PNT2 should be cultivated in is RPMI 1640 + 2mM Glutamine + 6-10 percent Foetal Bovine Serum (FBS) at 37°C + 5 percent CO2 [15]. The cells should be planted at roughly 2-4 x 104 cells/cm^2 and should be passaged when the subculture is between 70-80 percent confluent using 0.25 percent trypsin or trypsin/EDTA. These cells should be handled under laboratory containment level 2 [16].

RWPE1 Cells

Research into the etiology of prostate cancer and benign tumors of the prostate in the United States has been hindered due to the difficulties of acquiring fresh human tissue and the dearth of well-characterized cell lines that display development and differentiation features of normal prostatic epithelium. Male prostatic epithelial cells from a non-neoplastic source were immortalized with human papillomavirus to create the RWPE-1 cell line [17]. For the RWPE-2 cell line, derived from RWPE-1, was transformed using v-Ki-ras. Both RWPE-1 and RWPE-2 cells were shown to contain cytokeratins 8 and 18, which are associated with luminal prostatic epithelial cells, but they mostly co-express basal cell cytokeratins [17]. In reaction to the synthetic androgen mibolerone, these cell lines display growth stimulation, PSA and androgen receptor (AR) expression, establishing their prostatic epithelial origin. When exposed to EGF and bFGF, the RWPE-2 cells are more sensitive to stimulation, but when exposed to TGF-beta they are less receptive. Injection of RWPE-1 cells into naked mice, with or without Matrigel, does not cause the cells to proliferate in agar or create tumors [19-34]. Nude mice develop tumors from RWPE-2 cells, which grow as colonies on agar. RWPE-1 cells do not invade in the in vitro invasion experiment, while RWPE-2 cells do [34]. Both cell lines showed varying levels of nuclear p53 and Rb protein expression. Cell culture models of RWPE-1 and RWPE-2 cells may be used to study the control of prostate growth and carcinogenesis, respectively [34].

CWR-R1ca Prostate Cancer Cell Line

In terms of male cancer deaths, the top cause is prostate cancer [18]. Androgen receptor (AR-H874Y) in CWR-R1 cells is functional and activated at low doses of testosterone or dihydrotestosterone (DHT), with a single mutation (AR-H874Y) (DHT) AR-FL, AR-V7, and PSA mRNA and protein are expressed in cells. In a monolayer, cells may be propagated for more than 50 passages with low concentrations of DHT, cell line is an epithelial-stromal fibroblast co-culture. It is the development of prostate cancer, a disease of the male reproductive system, which affects the prostate. The AR is a focus for many anti-cancer research investigations because it promotes prostate cancer cells to thrive [19]. Normal prostate growth and maintenance depends on the AR, as does prostate cancer survival and advancement. These anti-androgen therapies, which are now used in the management of advanced disease prostate cancer, bind to the AR binding region and reduce or block androgen production [20]. The initial response to androgen deprivation treatment is positive, but most patients ultimately revert to a more severe, castration-resistant prostate cancer (CRPC), which is caused by the ongoing transactivation of AR. Developed from the castration-resistant or recurrent CWR-R1 prostate cancer cell line, in the beginning, the CWR-R1 cell line was obtained from the recurrent human xenograft tumors from murine 140-160 days after sterilization and expresses AR full length (AR-FL), AR-V7, and the mRNA and protein for prostate-specific antigen. When castration fails to eradicate prostate cancer, the CWR-1Ca cell line may be used to generate fibroblast-free cell lines that are resistant to the treatment [19]. Multiple rounds of brief trypsinization, cloning as well as pooling single-cell colonies were used to remove fibroblasts from the original parental CWR-R1 cells [19]. When androgen is used to stimulate cell proliferation, the CWR-1ca cells express the androgen receptor AR-FL as well as its splice variant AR-V7 [20].

LNCaP Cell Line and Its Derivatives

Due to a lack of cell lines to investigate pre-clinical prostate cancer, researchers were constrained in their ability to discover new treatments. previously, there was a lack of cell lines that adequately represent the clinical development of prostate cancer in humans [24]. Horoszewicz, et al. first described the formation of subcutaneous tumors in intact male athymic nude mice by using LNCaP, a cell line obtained from a metastatic lymph node lesion of human prostate cancer that is AR positive and androgen-sensitive [24]. The initial source of the LNCaP cell line was a metastatic prostate cancer patient's lymph node. LNCaP has been used to generate a plethora of cell lines for research into the development of prostate cancer [25]. Subcutaneous injections of LNCaP and its derivatives into male athymic nude mice do not cause metastasis. JHU-LNCaP-SM cells developed swiftly into tumors in intact male athymic nude mice with a 100% (13/13) tumor take rate. Five days after inoculation, tumors were visible, but tumor-free LNCaP-infected mice failed to develop tumors (0/15) over the same timeframe. Mice with developed tumors larger than 300 mm3 were surgically castrated to examine the androgen independence of JHU-LNCaP-SM tumor xenografts. A lack of tumor volume variation was seen in both groups, which suggests that treatment with androgen does not affect the rate of exponential development [25].

When it comes to men's malignancies, prostate cancer is the most prevalent and the second most common cause of cancer-related fatalities. Patients with advanced prostate cancer may benefit greatly from androgen restriction treatment, since androgen signaling is critical to prostate cancer development and antiapoptotic capabilities [26]. But even after an initial response to androgen restriction treatment, castration-resistant prostate cancer (CRPC) develops, leading to its recurrence and/or progression. Patients with advanced prostate cancer have been given novel AR-targeted medicines, such as enzalutamide (ENZ), as well as an anti-cancer chemotherapeutic agent, called Cabazitaxel [24,25]. However, these medications have been shown to have poor treatment effectiveness. Although the majority of CRPC tumors display AR-dependent development by activating AR mutations, amplification, or splice variants, up to 10-20 percent of CRPC cancers remove their AR reliance to avoid AR-targeted treatment are also present. AR-positive adenocarcinomas may become AR-negative small cell neuroendocrine prostate carcinomas, a symptom of this process (NEPCs). D growth, high-throughput screening, and development of xenograft tumors for in vivo testing are essential tools for discovering the determinants of therapy response and resistance [26]. However, contemporary cancer cell lines have a few drawbacks that must be considered. In vitro culture-grown tumor cell lines are used to create new cell lines based on already existing ones. Cancer cell lines produced by this method are not representative of the wide range of human malignancies [26]. There is little variability among PCa cell lines generated in monolayer cultures compared to those obtained from patient tumors. The NCI-60 cell line and its 60 human panel have been withdrawn by the National Cancer Institute of the United States.

22Rv-1 Cells

22Rv-1 cell is a human prostate cancer epithelial cell line that was generated from the xenograft of a CWR22 xenograft that was castrated and relapsed in mice before being serially reproduced in mice [27]. Prostate specific antigen (PSA) is expressed in the cell line. By Western blot examination, dihydroxytestosterone very slightly increases growth, although lysates are immunoreactive with antibodies to the androgen receptor [28]. Transforming growth factor beta-1 does not limit growth but rather stimulates it (TGF beta- 1). Human retrovirus XMRV has recently been shown to be highly titrated in 22Rv1 prostate cancer cells (xenotropic murine leukemia virus-related virus). Researchers often employ the 22Rv1 xenograft mouse cell line and in vitro cell culture tests to investigate the carcinogenesis of prostate cancer. XMRV, a gammaretrovirus, has recently been shown to be integrated into the genome of this cell line. When compared to CWR22, the xenograft cell lines 22Rv1 and CWR-R1, both of which include retroviruses in their supernatant, have been shown to be infected with gammaretrovirus [30]. XMRV has been shown to infect human cells in vitro, despite the fact that it

was most likely created by recombination processes in cell culture, and 22Rv1 and CWR-R1 cells are now deemed biosafety reagents [28]. When compared to the original cell line, 22Rv1 cells with reduced retroviral transcription exhibit lower tumor angiogenesis and enhanced necrosis of the main tumor formed by xenografted cells in SCI mice. When XMRV transcripts are present, osteopontin (OPN), CXCL14, IL13, and TIMP2 production in 22Rv1 cells rises considerably. Cell invasion and differentiation studies carried out in vitro provide further evidence to back up these findings [28]. As a result of our findings, we believe that 22Rv1 features like as migration, invasion, and tumor angiogenesis are at least partly influenced by the presence of XMRV transcripts. Prostate cancer cell lines containing xenotropic gammaretroviruses, such as 22Rv1 and other cell lines evaluated for viral sequences, should be carefully regulated.

Du-145 Cells

Human prostate cancer cell line DU145 is also known as DU-145 [31]. There are three primary prostate cancer cell lines that are employed in therapeutic research: DU145, PC3, and LNCaP. Cell lines DU145, PC-3 and LNCaP have all been generated from metastatic prostate cancer lesions in the brain, bone and lymph node tissues, respectively [25]. Different tumor microenvironments and origins of various cell lines have resulted in diverse properties of these cells [32]. Prostate-specific antigen is expressed in DU145 cells, which are unresponsive to androgen. These are typical of prostate cancer lesions that are difficult to cure.

A decrease in CDK2 and CDK4 activity, as well as in cyclin A and cyclin D1 levels, are all associated with G1 phase arrest in DU145 prostate cancer cells when IAA is added [31]. EGF Receptor overexpression is common in advanced prostate cancer. Cetuximab therapy has been shown to improve radiation sensitivity in the prostate cancer cell line DU145 in vitro; however, there are not enough clinical data to back this up.

Combining radiation and cetuximab therapy reduces cell proliferation in the DU 145 prostate cancer cell line, whereas cetuximab treatment alone had little effect. In a proliferation experiment, DU145 cells seemed to be more resistant to radiation and less responsive to cetuximab. Human prostatic cancer cell line DU145 (also known as DU-145) The standard prostate cancer cell lines utilized in therapeutic research include DU145, PC3, and LNCaP. It was shown that DU145 cells had a much greater GSH concentration and GSH/GSSG ratio compared to PC3 cells. DU145 cells also showed substantial increases in the basal and stimulated levels of Nrf2 and the genes it depends on.

PC-3 Cell and PC-3M Cells

Human prostate cancer bone metastases were used to isolate the PC3 cell line, which had a low degree of differentiation [34]. In spite of its modest metastatic potential, it lacks endogenous androgen receptors, making it a prostate cancer cell that is androgen-independent [34]. Research into androgen-resistant prostate cancer relies on the PC3 cell line. In the study of prostate cancer, PC3 (PC-3) is a human prostate cancer cell line. Biochemical alterations in advanced prostate cancer cells and their response to chemotherapeutic drugs may be studied using PC3 cells. Viral infection of immune-responsive mammalian cells is also studied using PC3 cells. In 1979, a 62-year-old Caucasian man was diagnosed with grade IV prostate cancer, and the PC3 cell line was created from his bone metastases. Androgens and glucocorticoids have little effect on these cells but data show that they are impacted by epidermal growth factors. Subcutaneous tumor xenografts of PC3 cells in mice may be employed for research into the tumor environment and therapeutic medication functionality [34]. The metastatic potential of PC3 cells is more than that of DU145 cells, which is moderate, and greater than that of LNCaP cells, which is low. The protein expression of PC3, LNCaP, and other cells has indicated that PC3 is typical of small cell neo endocrine cancer (25). Testosterone-5-alpha reductase and acidic phosphatase activity in PC3 cells is minimal, and they exhibit no PSA (prostate-specific antigen). Furthermore, a karyotypic examination of PC3 revealed that the cells had 62 chromosomes, making them almost triploid. The absence of a Y chromosome was revealed by Q-band analysis. PC3 cells exhibit hallmarks of a weakly differentiated adenocarcinoma, according to electron microscopy findings. There are many microvilli, junctional complexes, aberrant nuclei and nucleoli, abnormal mitochondria, annulate lamellas, and lipoidal structures in these cells [35,36].

General Comments for the Cells

There is still a need for a reliable, early detection method for prostate cancer, despite several molecular tests being developed in recent years and some receiving FDA approval. As a result, the hunt for new, more specific, as well as cost-effective biomarkers that may enhance early detection of prostate cancer and more accurately predict its clinical course is an important research objective. It is possible for cancer cells to alter several homeostatic processes in the body, resulting in changes in the synthesis, usage, and levels of many metabolites. Metabolomics is a potent analytical tool in oncology that may identify new biomarkers and therapeutic targets. Non-invasive samples may be studied using a metabolomic technique to find biochemical markers and, as a result, discrepancies between cancer as well as healthy metabolic phenotypes. Metabolomics may be used to intervene early since metabolic changes are thought to precede the growth of neoplastic cells. Biofluids (e.g., urine and serum/plasma), tissues, and cell lines are the most prevalent matrices employed in prostate cancer metabolomics investigations. Biofluids and tissues, in particular, might have metabolic profiles that are influenced by variables other than cancer cell metabolism, such as age, food, medicines, or chronobiological fluctuations; this must be considered when working with these types of matrices in order to produce accurate findings. In contrast, studies using cultured cell lines offer significant benefits over the use of urine or plasma, overcoming these drawbacks. There are several benefits to the use of pre-clinical investigations using cell lines, such as the

ability to exclude several significant confounding variables, such as age and nutrition. Because cell lines have a fixed state, they may be used to analyze a specific metabolic condition.

Consequently, we think that cell lines are the appropriate matrix to generate hypotheses about cellular processes and to uncover metabolic abnormalities that are not visible in research utilizing animal models or human patients because of their biological complexity. There are a few drawbacks to this in vitro model, however, such as a lack of cell–cell interactions between cultured cells and the tumor microenvironment, which is critical for the metabolic changes that occur during tumor progression. Because of this, the results of in vitro research need to be confirmed and validated in biofluids from patients with prostate cancer. Immortal cell lines are widely utilized in research in lieu of primary cells. They provide various benefits, such as they are cost efficient, simple to utilize, give an endless supply of material and circumvent ethical considerations related with the use of animal and human tissue. Cell lines can give a pure population of cells, which is useful as it delivers a consistent sample and repeatable findings. There are several papers employing cell lines as well as the American Type Culture Collection (ATCC) Cell Biology Collection which includes of cell lines [37-41] Cell line popularity may be judged from the numerous publications using cell lines. However, while being a strong tool, one must be cautious when employing cell lines in lieu of source cells. Cell lines should express and preserve functional properties as near to primary cells as feasible. This may especially be difficult to ascertain since frequently the roles of the main cells are not totally known. Since cell lines are genetically altered this may affect their phenotypic, natural functions and their reactivity to stimuli. Serial passage of cell lines may further produce genotypic and phenotypic diversity over a long period of time and genetic drift can also cause variability in cultures at a single point in time. Therefore, cell lines may not effectively mimic primary cells and may produce different outcomes.

Conclusion

It is clear that cell lines are an excellent alternative to primary cells in many ways. To be clear, cell lines don't exactly replicate primary cells. Therefore, careful consideration must be given to the design of investigations in order to ensure that results obtained by using cell line are solid. Primary cells should be used to duplicate important research. As a final point, it's important to acknowledge that studying primary cells and cell lines in an in vitro setting deprives them of important interactions with other cell types that might be vital to testing a theory. There are several studies showing that Sertoli cells interact with different cell types in the surrounding environment, which makes them especially sensitive to isolation or enrichment.

Acknowledgements

Authors AAN and SAA, contributed equally to this work, are supported by a Ph.D scholarship from king Saud Bin Abdulaziz University for Health Sciences, College of Science and Health Professions, Jeddah, Saudi Arabia.

References

1. Huxley J (1956) Cancer biology: comparative and genetic. Biol Rev Camb Philos Soc 31: 474-514.
2. Rasnick D (2012) The chromosomal imbalance theory of cancer. Boca Raton, FL, CRC Press, Taylor and Francis Group, USA.
3. Cheung PY, Deng W, Man C, Tse WW, Srivastava G, Law S, et al. (2010) Genetic alterations in a telomerase-immortalized human esophageal epithelial cell line: implications for carcinogenesis. Cancer letters 293(1): 41-51.
4. Bodnar AG, Ouellette M, Frolkis M, Holt SE, Chiu CP, (1998) Extension of life-span by introduction of telomerase into normal human cells. Science 279(5349): 349-352.
5. Mondello C, Chiesa M, Rebuzzini P, Zongaro S, Verri A, et al. (2003) Karyotype instability and anchorage-independent growth in telomerase-immortalized fibroblasts from two centenarian individuals. Biochemical and biophysical research communications 308(4): 914-921.
6. Weinberg RA, Weinberg RA (2006) The biology of cancer. WW Norton & Company.
7. Risbridger GP (2015) Human Cell Lines as Tools of Our Trade:"Laying It on the (Cell) Line". Molecular Endocrinology 29(1): 1-2.
8. Siegel RL, Miller KD, Jemal A (2018) Cancer statistics 2018. CA: a cancer journal for clinicians 68(1): 7-30.
9. Kwak JT, Hong CW, Pinto PA, Williams M, Xu S, et al. (2015) Is visual registration equivalent to semiautomated registration in prostate biopsy?. BioMed research international.
10. Bhatia B, Jiang M, Suraneni M, Patrawala L, Badeaux M, et al. (2008) Critical and distinct roles of p16 and telomerase in regulating the proliferative life span of normal human prostate epithelial progenitor cells. Journal of Biological Chemistry 283(41): 27957-27972.
11. Blagosklonny MV (2003) Cell immortality and hallmarks of cancer. Cell Cycle 2(4): 295-298.
12. Small MB, Gluzman Y, Ozer HL (1982) Enhanced transformation of human fibroblasts by origin-defective simian virus 40. Nature 296(5858): 671-672.
13. Khorchide M, Lechner D, Cross HS (2005) Epigenetic regulation of vitamin D hydroxylase expression and activity in normal and malignant human prostate cells. The Journal of steroid biochemistry and molecular biology 93(2-5): 167-172.
14. Souza AG, B Silva IB, Campos-Fernández E, Marangoni K F, Bastos VA, et al. (2018) Extracellular vesicles as drivers of epithelial-mesenchymal transition and carcinogenic characteristics in normal prostate cells. Molecular carcinogenesis 57(4): 503-511.
15. Gazzano-Santoro H, Ralph P, Ryskamp TC, Chen AB, Mukku VR (1997) A non-radioactive complement-dependent cytotoxicity assay for anti-CD20 monoclonal antibody. Journal of immunological methods 202(2): 163-171.
16. Elgass S, Cooper A, Chopra M (2014) Lycopene treatment of prostate cancer cell lines inhibits adhesion and migration properties of the cells. International journal of medical sciences 11(9): 948.
17. Meng H, Shen Y, Shen J, Zhou F, Shen S, (2013) Effect of n-3 and n-6 unsaturated fatty acids on prostate cancer (PC-3) and prostate epithelial (RWPE-1) cells in vitro. Lipids in health and disease 12(1):1-4.
18. Ballentine Carter H, Coffey DS (1990) The prostate: an increasing medical problem. The prostate 16(1): 39-48.

19. Gregory CW, Whang YE, McCall W, Fei X, Liu Y, (2005) Heregulin-induced activation of HER2 and HER3 increases androgen receptor transactivation and CWR-R1 human recurrent prostate cancer cell growth. Clinical Cancer Research 11(5): 1704-1712.

20. Shourideh M, DePriest A, Mohler JL, Wilson EM, Koochekpour S (2016) Characterization of fibroblast-free CWR-R1ca castration-recurrent prostate cancer cell line. The Prostate 76(12): 1067-1077.

21. Marchiani S, Tamburrino L, Nesi G, Paglierani M, Gelmini S, et al. (2010) Androgen-responsive and -unresponsive prostate cancer cell lines respond differently to stimuli inducing neuroendocrine differentiation. Int J Androl 33(6): 784-793.

22. Sherwood ER, Berg LA, Mitchell NJ, McNeal JE, Kozlowski JM, et al. (1990) Differential cytokeratin expression in normal, hyperplastic and malignant epithelial cells from human prostate. J Urol 143(1): 167-171.

23. Sramkoski RM, Pretlow TG, Giaconia JM, Pretlow TP, Schwartz S, et al. (1999) A new human prostate carcinoma cell line, 22Rv1. In Vitro Cell Dev Biol Anim 35(7): 403-409.

24. Horoszewicz JS, Leong SS, Chu TM, Wajsman ZL, Friedman M, Papsidero L, et al. (1980) The LNCaP cell line--a new model for studies on human prostatic carcinoma. Prog Clin Biol Res 37: 115-132.

25. Horoszewicz JS, Leong SS, Kawinski E, Karr JP, Rosenthal H, et al. (1983) LNCaP model of human prostatic carcinoma. Cancer Res 43(4): 1809-1818.

26. Castanares MA, Copeland BT, Chowdhury WH, Liu MM, Rodriguez R, et al. (2016) Characterization of a novel metastatic prostate cancer cell line of LNCaP origin. Prostate 76(2): 215-225.

27. Blank-Porat D, Gruss-Fischer T, Tarasenko N, Malik Z, Nudelman A, et al. (2007) The anticancer prodrugs of butyric acid AN-7 and AN-9, possess antiangiogenic properties. Cancer letters 256(1): 39-48.

28. Namekawa T, Ikeda K, Horie-Inoue K, Inoue S (2019) Application of Prostate Cancer Models for Preclinical Study: Advantages and Limitations of Cell Lines, Patient-Derived Xenografts, and Three-Dimensional Culture of Patient-Derived Cells. Cells 8(1): 74.

29. Yorukoglu K (2016) Current developments in uropathology. 1 ed: Turkiye Klinikleri J Med Pathol-Special Topics p. 35-40.

30. Namekawa T, Ikeda K, Horie-Inoue K, Inoue S (2019) Application of Prostate Cancer Models for Preclinical Study: Advantages and Limitations of Cell Lines, Patient-Derived Xenografts, and Three-Dimensional Culture of Patient-Derived Cells. Cells 8(1): 74.

31. Barranco WT, Eckhert CD (2006) Cellular changes in boric acid-treated DU-145 prostate cancer cells. British journal of cancer 94(6): 884-890.

32. Stone KR, Mickey DD, Wunderli H, Mickey GH, Paulson DF (1979) Isolation of a human prostate carcinoma cell line (DU 145). Int J Cancer 21(3): 274-281.

33. Kaighn ME, Narayan KS, Ohnuki Y, Lechner JF, Jones LW (1979) Establishment and characterization of a human prostatic carcinoma cell line (PC-3). Invest Urol 17(1): 16-23.

34. Tai S, Sun Y, Squires JM, Zhang H, Oh WK, et al. (2011) PC3 is a cell line characteristic of prostatic small cell carcinoma. Prostate 71(15): 1668-1679.

35. Pettersson A, Graff RE, Bauer SR, Pitt MJ, Lis RT, et al. (2012) The TMPRSS2: ERG rearrangement, ERG expression, and prostate cancer outcomes: a cohort study and meta-analysis. Cancer Epidemiol Biomarkers Prev 21(9): 1497-1509.

36. Chopra DP, Menard RE, Januszewski J, Mattingly RR (2004) TNF-α-mediated apoptosis in normal human prostate epithelial cells and tumor cell lines. Cancer letters 203(2): 145-154.

37. Bolin SR, Ridpath JF, Black J, Macy M, Roblin R (1994) Survey of cell lines in the American Type Culture Collection for bovine viral diarrhea virus. Journal of virological methods 48(2-3): 211-221.

38. Connolly JM, Rose DP (1990) Production of epidermal growth factor and transforming growth factor-α by the androgen-responsive LNCaP human prostate cancer cell line. The Prostate 16(3): 209-218.

39. Marcelli M, Cunningham GR, Haidacher SJ, Padayatty SJ, Sturgis L, et al. (1998) Caspase-7 is activated during lovastatin-induced apoptosis of the prostate cancer cell line LNCaP. Cancer research 58(1): 76-83.

40. Kovalenko PL, Zhang Z, Cui M, Clinton SK, Fleet JC, et al. (2010) 1, 25 dihydroxyvitamin D-mediated orchestration of anticancer, transcript-level effects in the immortalized, non-transformed prostate epithelial cell line, RWPE1. BMC genomics 11(1): 1-5.

41. Park SW, Kim JY, Kim YS, Lee SJ, Lee SD, et al. (2014) A milk protein, casein, as a proliferation promoting factor in prostate cancer cells. The World Journal of Men's Health 32(2): 76-82.

DOI: 10.32474/OAJOM.2021.05.000208