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Tomatoes against Tumors: Lycopene's Promise in Prostate Cancer Treatment

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Abstract
Lycopene, a carotenoid mainly found in tomatoes (*Solanum lycopersicum)*, is generally identified for its effective antioxidant properties and its strongest role in preventing and managing the disease, specifically prostate cancer. As a tetraterpene, lycopene is particularly useful at neutralizing free radicals, decreasing oxidative stress a essential element in cancer development Lycopene is typically present in the trans – isomer form in plants, however it converts to the more bioactive cis form in the human body. Prostate cancer is a serious health issue for the men worldwide, which often do not show symptoms in early stages, which complicates timely diagnosis. Lycopene's therapeutic result on prostate cancer has been noted in different studies, where it effectually hinder cancer cell proliferation, promotes apoptosis and decreases migration of cancer cell and invasion. Investigation shows that lycopene can increase the results of traditional treatments, like docetaxel chemotherapy, and enhance patient's quality life by relieving symptoms like urinary discomfort and bone pain. This analysis emphasizes lycopene's biochemical properties, its synthesis and its mechanism of action opposed to prostate cancer cells, featuring its promising role as a dietary and medicinal supplement in prostate cancer management. CREB3L4 regulates androgen receptor activity and may contribute prostate cancer proliferation through an AR-ER stress-CREB3L4 signaling pathways.

Keywords: Lycopene, Prostate Cancer, Anticancer Activity, CREB3L4 Protein

Introduction

Lycopene

Lycopene is a pigment which was first identified by the French botanist Alexis Millardet in 1876 inside tomato fruit and was later named by chemist C.A.Schunk. This is classified as a tetraterpene means consists of eight isoprene units and its molecular formula IS $C_{40}H_{64}$. Lycopene exists in two forms the trans- form which is present in plants and the cis form which is found in human blood. Lycopene is insoluble in water but it is soluble in various organic solvents like chloroform, hexane, acetone, benzene, methylene chloride and petroleum ether. Lycopene is a carotenoid nutraceutical and also known for its role in boosting defences against cancer, hypertension, cardiovascular conditions, hypertension as well as the inflammatory and neurodegenerative diseases. It primarily exists as the trans- isomers and is found in varying amounts in tomatoes, and also includes other sources such as watermelons, pink guava, apricots red bell peppers, grapefruits, red carrots and papayas. The lycopene concentration in tomatoes varies from 0.88 to 7.74 mg per 100gms affected by the tomato species and its stage of ripeness. When subjected to heat, lycopene can undergo cis isomerization which improves it bioactivities. The levels of lycopene mixture are determined by the various factors such as body weight, age, gastrointestinal health, lifestyle choices and food consumption. Bulky molecules like pectins can block up the absorption of lycopene, whereas fat build up. Therefore, dietary supplements containing oil-based lycopene might be more effectual than obtaining it from food sources. Lycopene does not reveal pro –vitamin A activity, still it carry 11 conjugated double bonds which result in satisfying rate constant with single oxygen that is dual that of beta-carotene. This leads to its defensive function against reactions that can activate carcinogenesis. our study provided considerable confirmation for the anti-cancer effects of lycopene in prostate cancer cell lines. Particularly, lycopene shows a double effect on a oxidative processes. While it has antioxidant properties, it may also determine a pro-oxidative effect during oncogenesis that helps in the removal of abnormal of abnormal cells. *In vitro* research has shown that lycopene exhibits anti-neoplastic properties by disturbing cancer cell migration, invasion, blood vessel formation and microenvironment regulation, while also encouraging apoptosis [1].

Biosynthesis of lycopene in tomato

The biosynthesis of lycopene in plants cells has been explained through the carotenoid synthesis metabolic pathway in the model organism Arabidopsis thaliana established in 1980.The initial step in the carotenoid biosynthesis pathway involves the conversion of the 20 – carbon geranyl geranyl pyrophosphate into the symmetrical 40-carbon molecule phytoene. Phytoene later go through four desaturation reactions, resulting in the formation of phytofluence, which is then converted into zeta-carotene, continued by neurosporene and eventually leads to the production of lycopene. Cyclization reactions takes place at the both ends of the lycopene molecule that leads to the formation of β-carotene, which then act as a precursor for the synthesis of xanthophylls, the oxygenated carotenoids. As a result, lycopene serves a precursor for both β-carotene and lutein. As carotenoids share a common pathway of synthesis of carotenoids, tomatoes may also contain trace amount of other carotenoids.

Lycopene is produced in the chromoplasts of the fruits cells, with the highest concentrations usually found in the pericarp cells near to the epidermis, compared to inner tissues of tomato. In tomatoes, dull ripening occurs between 40 to 60 days after planting, during which chloroplast change to chromoplast upon synthesis of lycopene.

Prostate

The prostate gland, a part of the male reproductive system, is located underneath the bladder and anterior of the rectum. It encloses the upper portion of the urethra, the tube responsible for transporting the urine from the bladder to penis. Behind the prostate the seminal vesicles are present, which is responsible to produce the fluid that forms part of semen. Anatomically, the prostate consists of two lobes on each side of central groove [2].

Prostate cancer

Prostate cancer arises from the cells of prostate gland. While numerous cell types are present in the prostate, almost all cases of prostate are classified as a adenocarcinoma, which arises from the glandular cells. Other forms of prostate cancer are extremely not common [3].

Generally, prostate cancer cells grow slowly and many people experience few or no symptoms until the disease has developed completely. Most of men diagnosed with prostate cancer eventually surrendered to unrelated health issues and many people remain unconcerned of their condition. Still, if prostate cancer begins to grow quickly or metastasizes over the prostate, it can become fully serious.

Epideomology

Incidence

The incidence of prostate cancer shows outstanding geographical and populational- based differences [4]. In 2018, a total of 1,276,106 new prostate cancer cases was recorded globally, registered for 7.1% of all male cancers [5]. The global distribution of prostate cancer incidence rates is highly unbalanced. Oceania had the top most age standardized rate (ASR) at 79.1 per 100,000 people followed by North America at 73.7 and Europe at 62.1 [4]. In comparison,the rates in Africa and Asia were much lower at26.6 and 11.5 respectively. The difference in incidence was prominent, with a 190-fold difference observed between the population with the highest rate(Guadeloupe, France, at 189.1) and the lowest rate (Bhutan at 1.0). The probability of developing prostate cancer increases considerably with age [9]. Although the diagnosis rate is comparably low about 1 in 350 men under 50 years old. The rate increases notably to 1 in 52 for those aged 50 to 59. Besides, 60% of men over is age of 65 are affected by the disease [6]. The reasons behind these differences in prostate cancer incidence across countries remain confusing. Still, the global difference in diagnosis rates may be related to the prevalence of PSA testing [7].

Mortality

Globally mortality rates for prostate cancer shoe remarkable dissimilarity across different regions [9]. in 2018, Central America reported the highest mortality rate at 10.7 per 100,000 people, followed closely by Australia and New Zealand at 10.2 and the Western Europe at 10.2.(9) on the other hand, Asian countries showed the lowest rates, with South-Central Asia at 3.3, Eastern Asia at 4.7 and South Eastern Asia at 5.4 along with the Northern Africa at 5.8(9). Particularly, one third of all prostate cancer- related deaths occurred in Asia (33.09%, totaling 118,427) while, Europe accounted for 29.9% (107,314 deaths). Besides, the mortality rate associated with prostate cancer increases with age, with about 55% of all deaths occurring in individuals over 65 years old [9].

Prevelance

In a research 2950 men were involved aged 62 to 91, from this 449 individuals(15.2%) was diagonesed with prostate cancer, with 67 of these cases having a Gleason score of 7 or more, indicating a high aggressive form of the disease. The prevalance of prostate cancer changed by PSA levels 6.6% in men with a PSA of 0.5 ng/ml or lesser, 10.1 percent for levels between 0.6 to 1.0ng/ml, 17.0 percent for PSA levels between 1.1 to 2.0 ng/ml, 23.9% for those between 2.1 and 3.0 ng/ml, and 26.9% for PSA levels between 3.1 and 4.0 ng/ml. In addition, the proportion of high- grades cancers increased from 12.5% among men with a PSA of 0.5 ng/ml or decreased to 25.0% in those with PSA levels between 3.1 and 4.0 ng/ml [8].

Prostate cancer as a global health issue

Prostate cancer is classified as the second most common cancer diagnosed widely and a fifth leading cause of cancer-connected deaths among men. In 2020 it was accounted for approximately 1,414,000 new cases and 375,304 deaths. It is the most frequently diagnosed cancer in112 countries and primary cause of deaths in 48 countries [9]. The increasing load of prostate cancer is anticipated to rise because of certain like population aging and economic evolution [10].

The worldwide statistics for prostate cancer tell a notably rise in the number of cases, deaths and disability –adjusted life years (DALYS) from 1990-2019. The total occurrence of prostate cancer increase suddenly by 169.11%, increasing from almost 524,110 cases in1990 to around 1.41 million in 2019. Deaths attributed to the disease also showed a significant rise of 108.94% from 233,000 to 486,840 at the same time. Besides, the number of DALYS related with prostate cancer increased by 98.25%, rising from 4.36 million to 8.64 million.

In terms of rates, the age –standardized incidence rate(ASIR) for prostate cancer experienced a sudden increase, with an approximated annual percentage change(EAPC) of 0.26(95% confidence interval:0.14,0.37), rising from 34.13 per 100,000 in 1990 to 38.63 per 100,000 in 1990 to 3863 per 100,000 in 2019. Inversely, both the age -standardized mortality rate (ASMR) and the age-standardized death rate (ASCR) decreases. The ASMR decreased at an EAPC OF -0.75(95%Cl:-0.78,-0.67), declining from 18.13 per 100,000 in 1990 to 15.28 per 100,000 in 2019. Likewise, the ASDR fall, with an EAPC of -0.71(95% Cl:-0.78,-0.63), from 186.30 per 100,000 in 1990 to 244.07 per 100,000 in 2019.

Risk factors of prostate cancer

Prostate cancer risk factors can be classified into two groups such as modifiable factors and non modifiable factors. Non modifiable factors involve ethnicity, age and family history. In modifiable factors involve lifestyle choices such as diet, physical activity levels and obesity, smoking habits which will be affected by the individual behaviors [18].

Treatment and management

A healthy diet, especially which is rich in vegetables and fruits, is advantageous for overall health. These foods are rich in fiber, flavonoids, vitamin C and carotenoids [11]. Research signify the dietary choices can lead to a reduce in both in the incidence as well as mortality rates related with prostate cancer. The consuming of fruits and vegetable may help in weaken or even prevent the development of this cancer. Numerous plants contain a anticancer compounds such as isothiocyanates, isoflavones, dithiolthiones, carotenoids, and vitamin E. Although various studies have researched the link between diet and prostate cancer, the findings have been unpredictable [12]. Vegetarians appear to have a low risk of developing prostate cancer as it offers vitamin A and E [13]. Besides, many prostate tumors show sensitivity to harmones, with the presence of the dihydrotestosterone receptor can affect how these tumors respond to androgen deprivation therapy [14]. Involving in the physical activity along with the dietary supplements and specific dietary factors, it also may contribute in the of prostate cancer. For example selenium and vitamin E which reduce the risk of developing the disease [15]. Surgical treatment aims to excise the prostate, seminal vesicles and ampullae of the vasa deferentia with the goal of achieving tumor-free margins are obtained. Still, this goal is not achieved in more than 25% of cases. Radial prostatectomy is a procedure which is carried out, but complications such as erectile dysfunction and bladder control problems, affecting up to 20% of patients [16]. Finasteride helps to prevent prostate cancer and reduce the risk of death associated with disease.

A. Localized disease (Stages 1 and 2)
   1. **Surgery:** Radial prostatectomy involves the removal of the prostate, surrounding tissue and some lymph nodes. Risk factors of surgery: Age > 75 years, life expectancy<10 years.
   2. **Radiation therapy:**

B. Locally advanced disease (stage 3)
   1. **Surgery:** Possible intervention.
   2. **Radiation:** It includes external beam or brachytherapy frequently paired with hormonal therapy.
   3. **Hormonal blockade:** Immediate hormonal blockade may enhance quality of life.

C. Metastatic disease (stage4)
   1. **Hormone –sensitive disease:** It is a hormone therapy to lower testosterone, like orchiectomy.
   2. **Hormone –refractory disease:** Chemotherapy is needed with docetaxel plus prednisone(first line) or mitoxantrone plus steroids.

D. Increasing PSA after radiation or prosectomy
   1. **Risk assessment:** Increase level in PSA indicates treatment failure, with high –risk factors including seminal vesicle involvement.
   2. **Local control:** Post- surgery radiation provides local control but this does not provide survival benefit but cause more complications. After radiation, salvage surgery is occasionally carried out if it has high complications rates, with most patients receiving medical therapy instead.

Lycopene and prostate cancer

Lycopene's role in cancer treatment has been primarily investigated in prostate cancer. Where majority of studies exhibit positive outcome. Research shows that lycopene improves treatment effects in cases of locally advanced prostate cancer and decreases prostate cancer-specific mortality in men with a dangerous risk of spreading the disease [21, 28]. Lycopene has been found to slow the development of recurrence of prostate cancer, despite of the hormone sensitivity of the tumors [24, 19]. It has also increased the efficacy of docetaxel chemotherapy in patients with advanced castrate-resistant prostate cancer and helps to maintain the benefits of orchidectomy in the patients who are suffering with advanced metastatic prostate cancer [29, 30, 25]. Besides, lycopene provide an improved quality of life by relieving bone pain and by controlling lower urinary tract symptoms. In some studies it indicates that lycopene do not provide advantages in treating patients with early-stage prostate cancer, specially those with biochemically relapsed prostate cancer nor in those with advanced hormone-refractory prostate cancer. However, other three studies reported beneficial effects of lycopene in the treatment of last group [27]. Animal studies observed lycopene's therapeutic effects on prostate cancer noted positive results, which showed reductions in tumor volume and weight, decrease prostate cancer-specific mortality, increased apoptosis and prolonged cancer free- survival. One study found that combining lycopene with the docetaxel significant increase in the therapeutic effect, resulted in 98% increase in apoptotic cells compared to docetaxel alone [17]. In addition co-supplementation with vitamin E enhanced treatment outcomes, with advantages observed especially when both supplements were used together [20, 22, 23, 26, 31].

Creb3l4 protein

CREB3L4 protein (cAMP responsive element binding protein 3 like 4), also known as AlbZIP, Tisp40 or ATCE1, is a transcription factor embedded in the endoplasmic reticulum membrane that includes a bZIP domain [7]. CREB3L4 is specially present in high amounts in the prostate, with elevated levels seen in cancerous compared to non cancerous prostate cells [10, 11]. In specific, it is highly expressed in high –grade prostatic intraepithelial neoplasia(PIN) and towards all grades of adenocarcinomas, making it a dormant biomarker for differentiating between the benign and malignant prostate cancer [12]. Despite androgen is known to control CREB3L4 expression, its particular role in the progression and development of prostate cancer is not fully understood. In this analysis the function of CREB3L4 affects androgen receptor activity, suggesting a link between them and it is possible that AR – ER stress and CREB3L4 signaling axis both may a role in promoting cell proliferation of prostate cancer.

Conclusion

The estimation of lycopene extracted from the tomato (*solanum lycopersicum*) on the human prostate cancer PC3 cell line emphasizes its potential as a promising nutraceutical agent in the treatment and management of prostate cancer. As a carotenoid with strong antioxidant properties, lycopene not only helps to balance out free radicals but also reveals important anti cancer activities by preventing cancer cell migration, invasion and angiogenesis while facilitating apoptosis. The complex balance between its antioxidant and possible pro-oxidative effects throughout oncogenesis site lycopene as a unique compound in cancer therapy.

The biosynthesis of lycopene in tomatoes is well understood metabolic pathway, with the pigment accelerating its chromoplasts in fruits. Diet intake of lycopene-rich foods, specially tomatoes, has helped in decreasing the risk of developing prostate cancer, enhancing the importance of dietary choices in cancer prevention. Additionally, the geographical inequality in prostate cancer incidence and mortality rates suggest that lifestyle and dietary factors, including lycopene intake, play a important role in cancer outcome.

In spite of some conflicting proof regarding its effectiveness in specific stages of prostate cancer, most of the studies support the concept that a lycopene can increase treatment result, specially in locally advanced cases and in combination such as docetaxel. however, animal studies suggest that lycopene can decrease tumor burden and improve survival rates, supporting the need for further clinical investigations. Lycopene holds important promise as complementary approach in the treatment of prostate cancer. Continuous research is essential to explain its mechanisms of action, improve its application in clinical settings and discover its long-term effects on patient results, highlighting its role as a part of a complete approach in management of prostate cancer. It focuses on the potential role of CREB3L4 in regulating androgen receptor activity within LNCaP prostate cancer cells, indicating a possible signaling axis involving AR and ER stress that may increase cell proliferation. Besides considering lycopene's reported anti cancer properties, further investigation into its effects on CREB3L4 and AR signaling could give valuable insights into the therapeutic strategies for prostate cancer, specially in reducing the proliferation of androgen –dependent cancer cells.

References

1. International Journal of Agriculture Innovations and Research Volume 6, Issue 5, ISSN (Online) 2319-147.
2. SEER Training Modules. http://training.seer.cancer.gov/prostate/anatomy/ accessed on 1st June, 2015)
3. (https://cancerstaging.org/references-tools/quickreferences)
4. SEER Cancer Statistics Review, 1975-2013 [Internet]. National Cancer Institue, Bethesda, MD, 2016. Available from: https://seer.cancer.gov/csr/1975_2015/. Accessed 04 February 2019. [Internet]. SEER, 2018. Available from: https://seer.cancer.gov/explorer/application.php.
5. Quinn M, Babb P. Patterns and trends in prostate cancer incidence, survival, prevalence and mortality. Part I: international comparisons. BJU Int. 2002; 90(2):162-173.
6. Thompson IM, Pauler DK, Goodman PJ, Tangen CM, Lucia MS, Parnes HL, *et al*. Prevalence of prostate cancer among men with a prostate-specific antigen level≤ 4.0 ng per milliliter. New England Journal of Medicine. 2004; 350(22):2239-2246.
7. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, *et al*. 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
8. Culp MB, Soerjomataram I, Efstathiou JA, Bray F, Jemal A. Recent global patterns in prostate cancer incidence and mortality rates. Eur Urol. 2020; 77:38-52. Doi: 10.1016/j.eururo.2019.08.005
9. Garg M, Dalela D, Goel A, *et al*. Prevention of prostate cancer with vitamins-current perspectives. Asian Pac J Cancer Prev. 2014; 15:1897-1904.
10. Meng H, Hu W, Chen Z, *et al*. Fruit and vegetable intake and prostate cancer risk: A meta-analysis. Asian Pac J Clin Oncol. 2013; 10:133-140.
11. Klein E, Thompson I, Tangen C, *et al*. Vitamin E and the risk of prostate cancer: The Selenium and Vitamin E Cancer Prevention Trial (SELECT). JAMA. 2011; 306:1549-1556.
12. Klein E, Thompson I, Tangen C, *et al*. Vitamin E and the risk of prostate cancer: The Selenium and Vitamin E Cancer Prevention Trial (SELECT). JAMA. 2011; 306:1549-1556.
13. Wolk A. Diet, lifestyle and risk of prostate cancer. Acta Oncol. 2005; 44:277-281.
14. Zhi Z, Shi-Xin L, Tian Z. Abiraterone for treatment of metastatic castration-resistant prostate cancer: A systematic review and meta-analysis. Asian Pac J Cancer Prev. 2014; 15:1313-1320.
15. National Comprehensive Cancer Network (NCCN). Practice Guidelines in Oncology: Prostate Cancer. Version. 2014; 2. Accessed at: http://www.nccn.org/patients/guidelines/prostate/index.html on 18.06.2015)
16. Perdana NR, Mochtar CA, Umbas R, Hamid AR. The Risk Factors of Prostate Cancer and Its Prevention: A Literature Review. Acta Med Indones. 2016; 48(3):228-238. PMID: 27840359.
17. Tang Y, Parmakhtiar B, Simoneau AR, Xie J, Fruehauf J, Lilly M, Zi X. Lycopene enhances docetaxel's effect in castration-resistant prostate cancer associated with insulin-like growth factor I receptor levels. Neoplasia. 2011; 13:108-119. Doi: 10.1593/neo.101092. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
18. Boileau TW-M, Liao Z, Kim S, Lemeshow S, Erdman JWJ, Clinton SK. Prostate carcinogenesis in N-methyl-N-nitrosourea (NMU)-testosterone-treated rats fed tomato powder, lycopene, or energy-restricted diets. J. Natl. Cancer Inst. 2003; 95:1578-1586. Doi:

10.1093/jnci/djg081. [PubMed] [CrossRef] [Google Scholar]
19. Kristal AR, Till C, Platz EA, Song X, King IB, Neuhouser ML, Ambrosone CB, *et al*. Serum lycopene concentration and prostate cancer risk: Results from the Prostate Cancer Prevention Trial. Cancer Epidemiol. Biomark. Prev. 2011; 20:638-646. Doi: 10.1158/1055-9965.EPI-10-1221. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
20. Vaishampayan U, Hussain M, Banerjee M, Seren S, Sarkar FH, Fontana J, *et al*. Lycopene and soy isoflavones in the treatment of prostate cancer. Nutr. Cancer. 2007; 59:1-7. Doi: 10.1080/01635580701413934. [PubMed] [CrossRef] [Google Scholar]
21. Gann PH, Ma J, Giovannucci E, Willett W, Sacks FM, Hennekens CH, Stampfer MJ. Lower prostate cancer risk in men with elevated plasma lycopene levels: Results of a prospective analysis. Cancer Res. 1999; 59:1225-1230. [PubMed] [Google Scholar]
22. Morgia G, Voce S, Palmieri F, Gentile M, Iapicca G, Giannantoni A, *et al*. Association between selenium and lycopene supplementation and incidence of prostate cancer: Results from the post-hoc analysis of the procomb trial. Phytomedicine. 2017; 34:1-5. Doi: 10.1016/j.phymed.2017.06.008. [PubMed] [CrossRef] [Google Scholar]
23. Vogt TM, Mayne ST, Graubard BI, Swanson CA, Sowell AL, Schoenberg JB, *et al*. Serum lycopene, other serum carotenoids, and risk of prostate cancer in US Blacks and Whites. Am. J. Epidemiol. 2002; 155:1023-1032. Doi: 10.1093/aje/155.11.1023. [PubMed] [CrossRef] [Google Scholar]
24. Bowen P, Chen L, Stacewicz-Sapuntzakis M, Duncan C, Sharifi R, Ghosh L, *et al*. Tomato sauce supplementation and prostate cancer: Lycopene accumulation and modulation of biomarkers of carcinogenesis. Exp. Biol. Med. 2002; 227:886-893. Doi: 10.1177/153537020222701008. [PubMed] [CrossRef] [Google Scholar]
25. Rowles JL, Smith JW, Applegate CC, Miller RJ, Wallig MA, Kaur A, *et al*. Dietary Tomato or Lycopene Do Not Reduce Castration-Resistant Prostate Cancer Progression in a Murine Model. J. Nutr. 2020; 150:1808-1817. Doi: 10.1093/jn/nxaa107. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
26. Van Breemen RB, Sharifi R, Viana M, Pajkovic N, Zhu D, Yuan L, Yang Y, *et al*. Antioxidant effects of lycopene in African American men with prostate cancer or benign prostate hyperplasia: A randomized, controlled trial. Cancer Prev. Res. 2011; 4:711-718. Doi: 10.1158/1940-6207.CAPR-10-0288. [PMC free article] [PubMed] [CrossRef] [Google Scholar]
27. Clark PE, Hall MC, Borden LSJ, Miller AA, Hu JJ, Lee WR, *et al*. Phase I-II prospective dose-escalating trial of lycopene in patients with biochemical relapse of prostate cancer after definitive local therapy. Urology. 2006; 67:1257-1261. Doi: 10.1016/j.urology.2005.12.035. [PubMed] [CrossRef] [Google Scholar]
28. Asada R, Kanemoto S, Kondo S, Saito A, Imaizumi K. The signalling from endoplasmic reticulum-resident bZIP transcription factors involved in diverse cellular physiology. J Biochem. 2011; 149:507-518. [DOI] [PubMed] [Google Scholar]
29. Labrie C, *et al*. Androgen-regulated transcription factor AIbZIP in prostate cancer. J Steroid Biochem Mol Biol. 2008; 108:237-244. [DOI] [PubMed] [Google Scholar]
30. Qi H, *et al*. AIbZIP, a novel bZIP gene located on chromosome 1q21.3 that is highly expressed in prostate tumors and of which the expression is up-regulated by androgens in LNCaP human prostate cancer cells. Cancer Res. 2002; 62:721-733. [PubMed] [Google Scholar]
31. Levesque MH, El-Alfy M, Berger L, Labrie F, Labrie C. Evaluation of AIbZIP and Cdc47 as markers for human prostatic diseases. Urology. 2007; 69:196-201. [DOI] [PubMed] [Google Scholar]