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Decreased ABCG2 Expression in Prostate Cancer and Negatively Associated with Poorly Differentiated Grade and Biochemical Recurrence

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Summary

Few prognostic biomarkers have been identified for prostate cancer and there are clinical difficulties in distinguishing between relapsing and non-relapsing diseases. The aim of this study is to investigate the hypothesis that ABCG2 might be a potential biomarker for prostate cancer and could distinguish between aggressive tumours requiring radical intervention and those that have a good prognosis. ABCG2 is a transmembrane protein that plays a vital role in promoting proliferation and maintaining the undifferentiated phenotype of stem cells. It is thought to be a potential biomarker that can predict clinical progression and prognosis of different kinds of tumors. However, its role in prostate tumor remains unclear.

Nuclear and cytoplasmic ABCG2 staining has been evaluated by immunohistochemistry using two sources of patient samples. The tissue microarray group consists of 96 cases including normal, adjacent normal and malignant prostate tissue samples. The Bath cohort consists of 30 samples, including samples from patients that had recurrent disease and those who remained disease-free.

The immunohistochemical study showed nuclear and cytoplasmic ABCG2 expression in benign and malignant prostate samples. Cytoplasmic ABCG2 expression was also significantly reduced in prostate cancer compared to normal tissues. Cytoplasmic ABCG2 staining was negatively associated with increasing Gleason grade. In the Bath cohort, there was a negative association between ABCG2 expression and biochemical relapse. This preliminary data showed that ABCG2 might play a role in cancer formation and/or aggressiveness and warrants further investigation to understand its function and establish if it could be a potential diagnostic biomarker for prostate tumour.

Keywords: Prostate cancer, Biomarkers, ABCG2, IHC.

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Introduction

A prostate is the largest accessory gland in the male reproductive system. It is a glandular organ surrounding the neck of the urinary bladder and urethra and the normal weight of the adult prostate is about twenty grams (1). The histological architecture of the prostate shows that there are multiple epithelial glands surrounded by abundant fibromuscular stroma (2). Each epithelial layer of prostate contains three cell types; basal, secretory (luminal), and neuroendocrine cells (3&4). Surrounding the epithelial cells are several types of cells in the stromal layer of the prostate, including smooth muscle cells, fibroblasts, and myofibroblasts (5). There are three most common pathological disorders which affect the prostate glands, including prostatitis (inflammation of the prostate), benign prostate hyperplasia (BPH) (enlargement of the prostate gland) and cancers (1). This study will focus on prostate cancer (PCa) only.

PCa is a heterogeneous disease and represents a global healthcare issue that is mostly a diagnosis of elderly men (6). A few diagnostic and prognostic biomarkers have been identified for PCa, including prostate-specific antigen (PSA) (7). However, there is a need for more specific and sensitive biomarkers in PCa diagnosis and especially for measuring PCa prognosis, for example, to distinguish between relapsing and non-relapsing cases. Recently, potential stem cells found within a tumour have received a lot of attention and it is thought that these cells may have a role in cancer initiation, progression and drug resistance (8) . Cancer stem cells (CSCs) have been linked to PCa relapse (9), and so analysis of expression of proteins that have been linked to stem cells (SCs) represents an interesting new avenue for future biomarker studies. One of these proteins is ATP binding cassette group 2 (ABCG2)/ Breast cancer resistance protein (BCRP).

ABCG2, a member of the ABC transporter family, is a transmembrane protein that plays a vital role in promoting proliferation and maintaining the undifferentiated phenotype of stem cells (10). It is linked to drug-resistance and is thought to be a potential biomarker that can predict clinical progression and prognosis of different kinds of tumors, including breast cancer (11) as well as identifying CSCs (10). There are a number of publications that have studied ABCG2 protein or mRNA levels in normal and malignant tissues, different Gleason grade, clinical stage and biochemical relapse. Cytoplasmic ABCG2 expression was significantly reduced in PCa compared to normal prostate (NP) and seminal vesicle (12). In contrast, another study showed no significant difference in ABCG2 mRNA levels between normal and malignant prostate samples, using real-time PCR (9). In addition, increased cytoplasmic ABCG2 staining was observed in PCa tissues with a medium Gleason grade compared to those with either a lower or a higher Gleason grade (13). A previous study found ABCG2 levels in breast cancer significantly associated with clinical stage and lymph node metastasis (11). ABCG2 expression was not associated significantly with grades of breast and oesophageal squamous cell carcinomas (11&14). There was also no significant difference between ABCG2 levels and oesophageal squamous cell carcinomas stages (11). In terms of relapse, ABCG2 mRNA

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level was significantly increased in PCa relapse compared to non-relapsed (9) and was also higher in CRPC compared to metastatic PCa (15). The major goal of this study was to focus on the expression of ABCG2 and establish if they are differentially expressed between normal and malignant prostate tissues and/or between samples with different clinical features, including relapsing vs non-relapsing tumors.

Materials and methods

This retrospective study was covered by the National Health Service (NHS) ethical and research approval (REC reference: 13/WS/0153; IRAS project ID: 112241). In this study, two different sources of prostate samples were used, including a Bath and a tissue microarray (TMA) cohorts. A Bath cohort consists of 30 paraffin-embedded blocks (FFPE) of PCa, including those from patients who had, and had not, undergone recurrence, and 5 NP tissue samples, were obtained from the histopathological laboratories of the Royal United Hospital (RUH), Bath/ UK. The samples were collected between 1997 and 2018. TMA cohort (PR1921) had 96 cases, 80 of them were PCa, whereas, the rest were normal or normal tissues that were adjacent to the PCa, termed adjacent normal (8 cases for each). Each case was represented with two core tissue biopsies to form a total of 192 cores. This study also used normal liver tissues as positive controls. The clinical data of the patients in both cohorts are shown in Table 1.

Table 1: Clinical data of prostate sample in both cohorts.

Clinical data		TMA cohort %	Bath cohort%
Number of samples	Normal	16	5
	Malignant	80	30
Age range	Normal	21-68	31-62
	Malignant	20-85	58-81
Primary Gleason grade	3	13 (16.25%)	11 (36.6 %)
	4	46 (57.5%)	16 (53.3%)
	5	18 (23. 75)	0 (0%)
	ND	3 (2.5%)	3(10.1%)
T category	T1-T2	51 (63.8%)	16 (53.3%)
	T3-T4	28 (35%)	11 (36.6%)
	N/A	1 (1.2%)	6 (13.1%)
N category	N0	65 (81.2%)	22 (73.3%)
	N1	14 (17.5%)	3 (10%)
	ND	1(1.3%)	5 (16.7%)
M category	M0	64 (80%)	19 (63.3%)
	M1	15 (18.7%)	2 (0.1%)
	ND	1 (1.3%)	9(36.6%)
Biochemical recurrence status (at 5 years)	Non-Recurrent	N/A	8 (26.6%)
	Recurrent	N/A	16 (53.4%)
	N/A	N/A	6 (20%)

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Immunohistochemistry

Immunohistochemistry (IHC) staining was carried out using anti-ABCG2 mouse monoclonal antibody (Abcam, catalogue number Ab3380). 5um thick sections of prostate tissues were used on positive charge slides and were baked overnight at 37°C. Prior to IHC, deparaffinization and rehydration through graded ethanol series of decreasing ethanol concentration (100%, 95% & 70% respectively) for a minute each time were necessary to remove the paraffin from tissues and to rehydrate tissue samples, respectively. Tissues were then permeabilized with 0.5% Triton X-100 in phosphate buffer saline (PBS), subjected to heat-induced epitope retrieval in a Tris/EDTA buffer, pH 9 with 0.05% Tween 20 for 30 minutes at 90°C, and allowed to cool to room temperature for 20 minutes. Subsequently, the sections were incubated in 3% H_2O_2 (Dako peroxidase) at room temperature for 10 minutes, followed by rinsing gently three times with PBS buffer for 5 minutes each. After blocking for 30 minutes in 10% normal goat serum and 0.5% BSA in PBS, samples were treated with anti-ABCG2 antibody, dilution1:100 (Dako, Ely, UK) overnight at 4°C.

In the next day, immunodetection was performed using the EnVision+ Kit (K400611-2 and K401011-2, Dako, Ely, UK) following the manufacturer's instructions with DAB exposure for 5 minutes. The sections were counterstained with Vector Hematoxylin solution (H3401, Vector Laboratories, Peterborough, UK) at room temperature for a minute to stain the nucleus of cells. Slides then were rinsed thoroughly the running tap water for 3 minutes. To differentiate the hematoxylin stain, the slides were then soaked three times in 70% ethanol with 1% HCl. The slides were also immersed for a minute in an alkaline solution that was prepared by adding 1% ammonium hydroxide to 70% ethanol to restore the bluing stain of hematoxylin. At this point, the staining steps were finished. After that, the slides were washed with two changes of different ethanol concentration 95% and 100% for a minute. Slides were then washed twice with Histoclear for 2 minutes each. Next day, the slides were ready to examine under a light microscope (Nikon Eclipse E800) equipped with a Nikon digital camera (DS-U1 CCD).
For assessment of IHC staining, the whole sections were examined under a 20x objective to determine the nuclear and cytoplasmic expression of ABCG2 staining in prostate tissues. The sections were scored using a semi-quantitative scoring system as the following: the percentage of positive cells was scored as: (0: 0; 1: 1-25%; 2: 26-50%; 3:51-75%; and 4: 76-100%) and The intensity was graded as (0: negative, 1: weak, 2: moderate; and 3: strong). The final score represents the sum of the proportion and intensity scores, which ranged from 0 to 7 (16).

Statistical analysis

Statistical analysis was performed using GraphPad Prism version 6.00 for Windows, GraphPad Software, La Jolla California USA, www.graphpad.com, including mean, standard error and standard deviation values. Statistical analysis was carried out either using unpaired T-test and one-way ANOVA with Tukey's multiple comparisons tests. Results were considered significant if the P.value was ≤ 0.05.

Results

A) Immunohistochemical staining of ABCG2 in the normal and malignant prostate samples from both cohorts

ABCG2 immunostaining was analyzed using IHC in prostate samples from two independent cohorts. Both normal and malignant prostate tissues had membranous ABCG2 staining with variable levels of staining,

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ranging from strong and widespread (Figure 1, C, arrow) to moderate and scattered (Figure 1, A, arrow) or negative (Figure 1, E, arrow). Normal and malignant prostate tissue samples also had cytoplasmic ABCG2 staining and the intensity of signal varied widely, ranging from strong and widespread (Figure 1, C and 2, A, arrowheads), moderate (Figure 1, D and 2 C, D&E, arrowheads), weak (Figure 1 A, B& E, and 2, B&F, arrowheads), and negative (Figure 1, F, and 2, H, arrowheads). In addition, nuclear ABCG2 staining was observed in prostate tissues from both cohorts with different levels of staining, ranging from strong (Figures 1, B, and 2, A, arrows) to weak (Figure 1, F and 2, E arrows) or negative (Figure 1, D, and 2, B& G arrows). ABCG2 would not be predicted to be expressed in the nuclei of normal and malignant prostate tissues because it's a transmembrane transporter protein. This suggests that this staining might well be background, however, it was decided to quantify it as it might act as an internal control that would not be expected to be linked to any disease progression. ABCG2 is expressed in the membrane and cytoplasm of hepatocyte cells (18) and so this study used normal liver tissues as a positive control for ABCG2 and the IHC staining showed membranous (Figure 1, G, arrow) and cytoplasmic (Figure 1, G, arrowheads) ABCG2 staining in the hepatocyte cells. A negative control (no primary antibody) showed no significant background staining in prostate tissue (Figure 1, H, arrow).

B) Association between ABCG2 immunohistochemistry and histopathological parameters of prostate cancer in both cohorts

In order to evaluate if there was an association between ABCG2 immunostaining in normal vs. malignant prostate tissues and/or other PCa histopathological features, nuclear and cytoplasmic ABCG2 staining was quantified using a semi-quantitative score and then compared to histopathological and clinical parameters of PCa using the clinical data available for both cohorts.

The statistical analysis showed that cytoplasmic ABCG2 staining was significantly reduced in PCa compared to NP tissues ($p= 0.048$) (Figure 3, B & Table 2) and ($p= <0.0001$) (Figure 4, B, Table 3) in the Bath and TMA cohort, respectively. In addition, cytoplasmic ABCG2 staining was negatively associated with increasing primary Gleason grades in the TMA cohort ($p= 0.0004$) (Figure 4, D & Table 3). Analysis of IHC data using Tukey's multicomparison tests showed cytoplasmic ABCG2 staining significantly decreased in primary Gleason grade 5 tissues compared to those with a grade 4 (0.0387) or grade 3 ($p= 0.0003$), and also decreased significantly when comparing between PCa tissues with a grade 4 & 3 ($p= 0.0.364$) (Figure 4, D & Table 3). This negative association was observed in the bath cohort, but the result was not significant ($p=0.1199$) (Figure 3, D & Table 2). Cytoplasmic staining was not associated with a clinical stage in both Cohorts. In the Bath cohort, cytoplasmic ABCG2 staining was reduced significantly in PCa recurrent patients compared to those with a non-recurrent ($p=0.0141$) (Figure 3, H & Table 2).

The IHC quantification showed nuclear ABCG2 staining not associated significantly with PCa and other histopathological parameters, including Gleason grade and clinical stage and relapse (Figures 3 & 4), except in the bath cohort, nuclear ABCG2 staining was positively associated with increasing primary Gleason grade and clinical stage T ($p = 0.0221$& 0.0337 respectively) (Figure 3, C& E).

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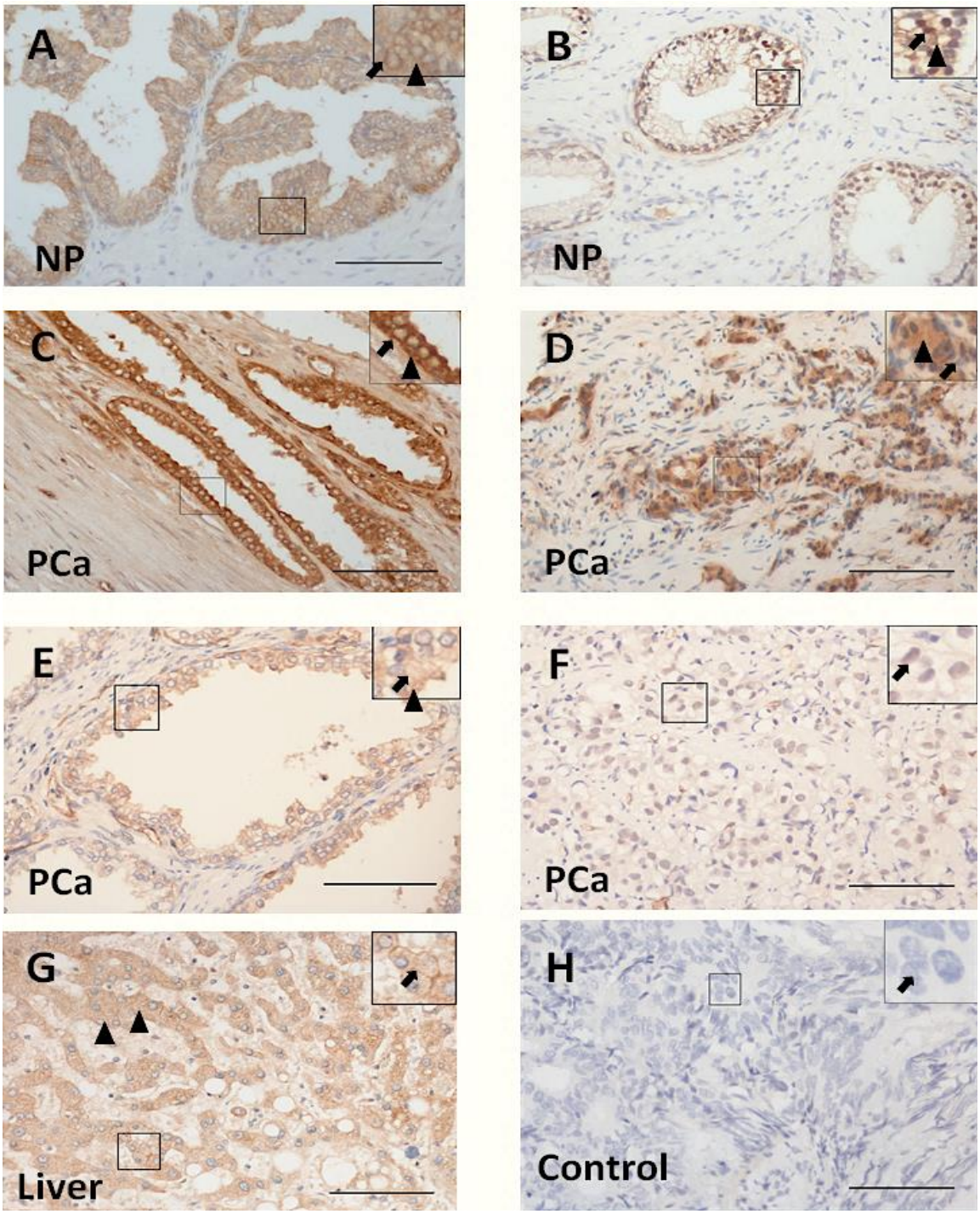

Figure 1: ABCG2 staining in samples from the Bath cohort. ABCG2 was stained heterogeneously in both normal and malignant tissues of the prostate. (A) Moderate membranous (Black arrow) and weak cytoplasmic (Black arrowhead) ABCG2 staining in NP. (B) Strong nuclear (Black arrow) and weak cytoplasmic (Black arrowhead) ABCG2 staining in NP. (C) Strong membranous (Black arrow) and cytoplasmic (Black arrowhead) ABCG2 staining in PCa. (D) Moderate cytoplasmic (Black arrowhead) and negative nuclear (Black arrow) ABCG2 staining in PCa. (E) Weak cytoplasmic (Black arrowhead) with negative nuclear ABCG2 staining in PCa. (F) Weak nuclear (Black arrow) and negative cytoplasmic ABCG2 staining in PCa. (G) Membranous (Black arrow) and cytoplasmic (Black arrowheads) ABCG2 staining in hepatocyte cells. (H) Negative control (no primary antibody added) showed no background staining (Black arrow) in PCa. Scale bars=100µm.

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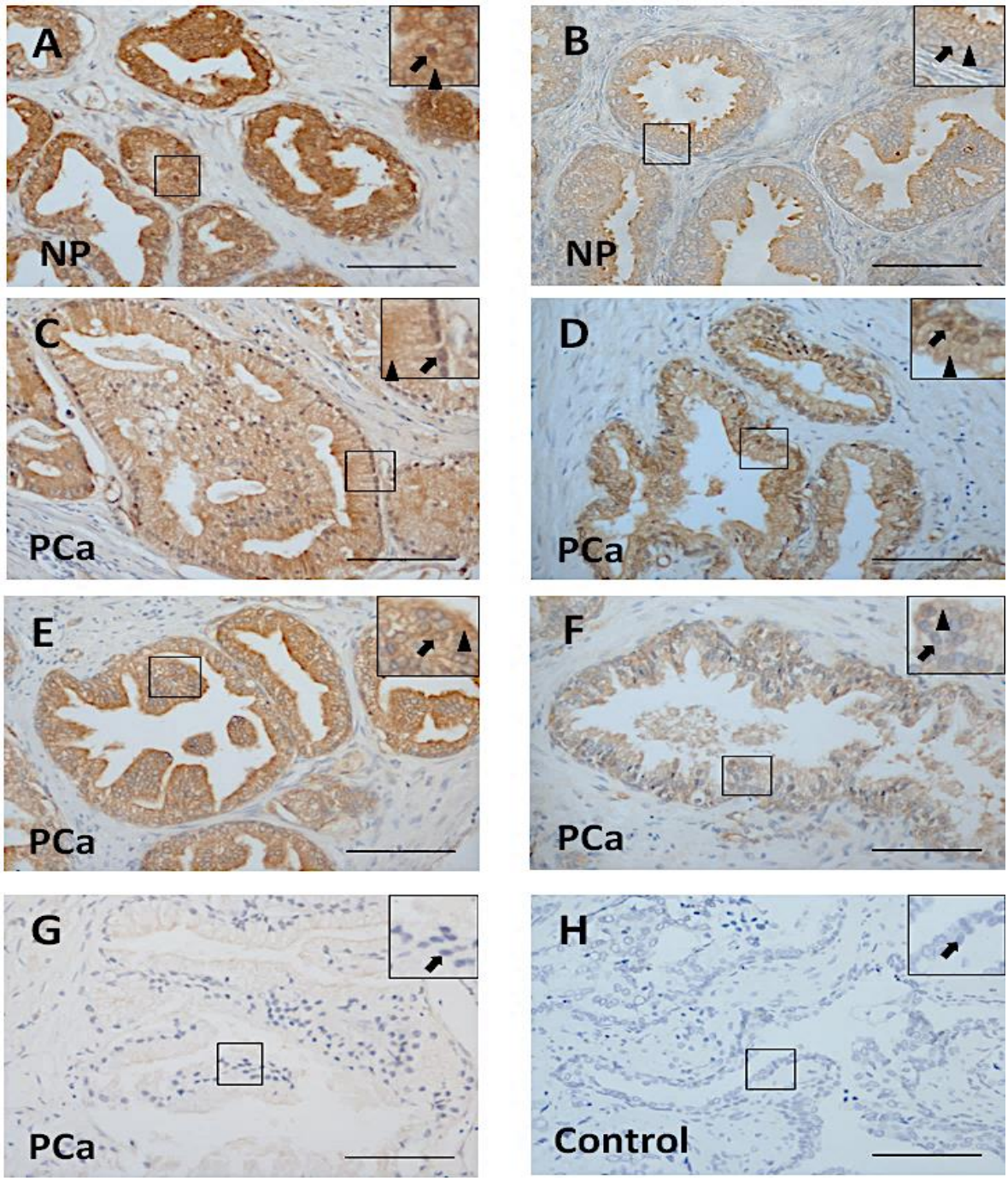

Figure 2: ABCG2 staining in samples from the TMA cohort. ABCG2 was stained heterogeneously in both normal and malignant tissues of the prostate. (A) Strong nuclear (Black arrow) and cytoplasmic (Black arrowhead) ABCG2 staining in NP. (B) Weak cytoplasmic (Black arrowhead) and negative nuclear (Black arrow) ABCG2 staining in NP. (C) Strong nuclear (Black arrow) and moderate cytoplasmic (Black arrowhead) ABCG2 staining in PCa. (D) Moderate nuclear (Black arrow) and cytoplasmic (Black arrowhead) ABCG2 staining in PCa. (E) Weak nuclear (Black arrow) and moderate cytoplasmic (Black arrowhead) ABCG2 in PCa. (F) Weak cytoplasmic (Black arrowhead) and negative nuclear (Black arrow) ABCG2 staining in PCa. (G) No significant staining for ABCG2 (Black arrow) in PCa. (H) Negative control (no primary antibody added) showed no background staining (Black arrow) in PCa. Scale bars=100µm.

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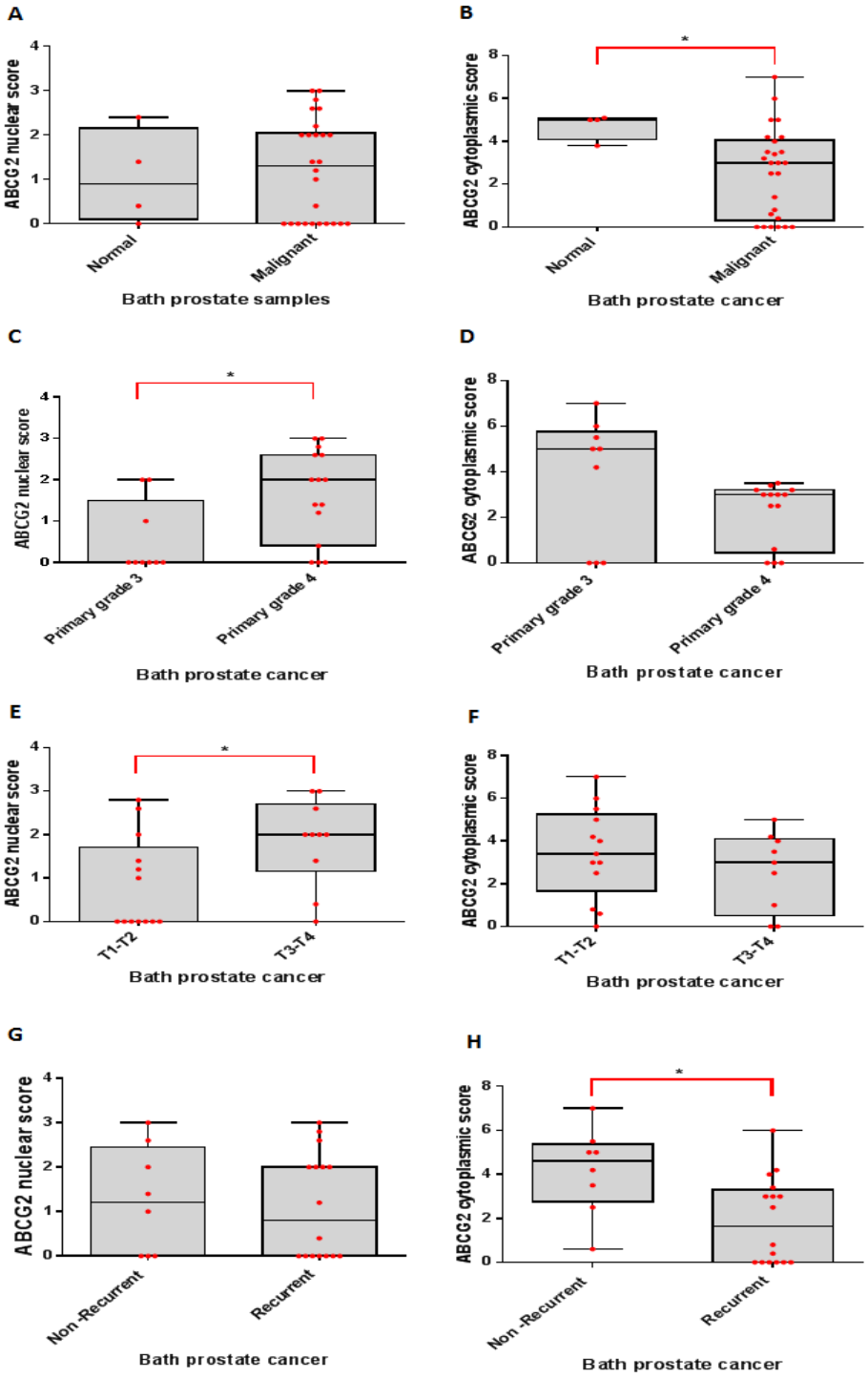

Figure 3 Quantification of nuclear and cytoplasmic ABCG2 staining in the Bath prostate tissue samples. Immunohistochemical staining of ABCG2 was quantified in the Bath cohort using the proportion and intensity 1 scores for nuclear and cytoplasmic IHC staining. (A) Nuclear ABCG2 staining showed no significant difference between normal and malignant prostate tissues (p= 0.7873). (B) Cytoplasmic ABCG2 staining was significantly reduced in PCa compared to NP tissues (p= 0.048). (C) Nuclear ABCG2 staining was positively associated with increasing primary Gleason grade (p=0.0221). (D) Cytoplasmic ABCG2 staining was negatively associated with increasing primary Gleason grade, but the results were not significant (p=0.1199). (E) Nuclear ABCG2 staining was positively associated with increasing clinical stage T (p=0.0337). (F) There was no association between cytoplasmic ABCG2 and clinical stage T (p=0.327). (G) There was no association between nuclear ABCG2 and risk of recurrence (p=0.8106). (H) Cytoplasmic ABCG2 staining was negatively associated with a risk of recurrence (p=0.0141). The mean of five random fields was taken per prostate sample. Statistical significance was determined with unpaired T-test for each set of conditions. NP (n=5), PCa (n=30), grade 3(n=11), grade 4(n= 16), T1-2 (n=16), T3-4 (n= 11), recurrent PCa (n=16), non- recurrent PCa (n=8).

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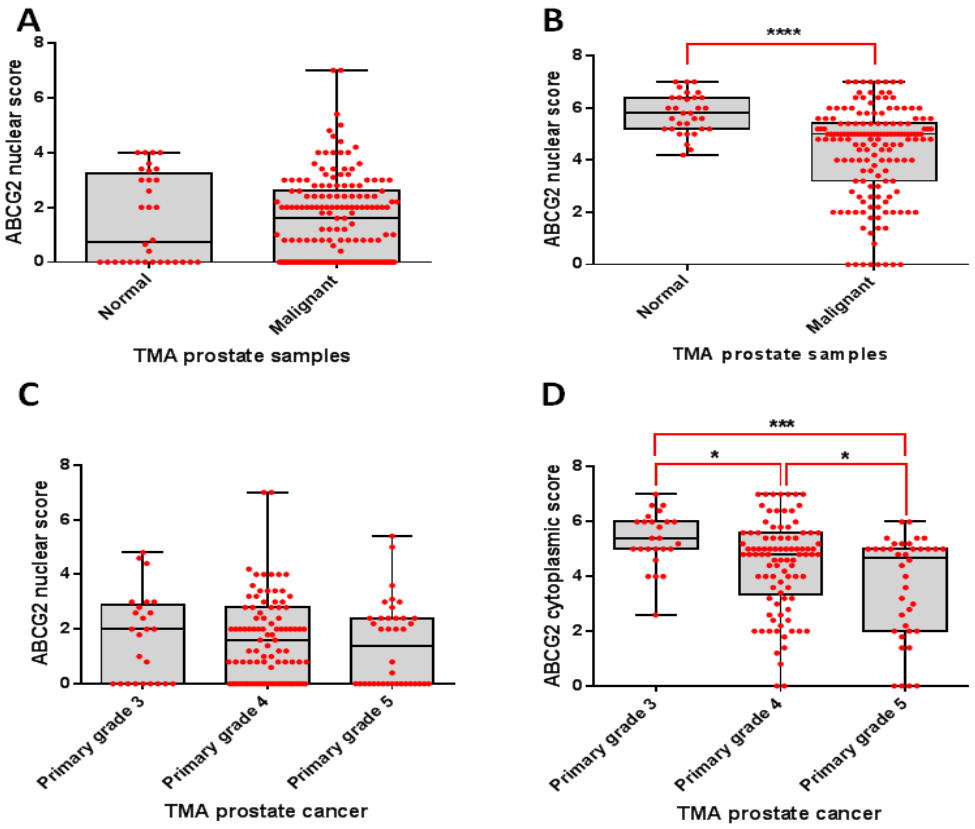

Figure 4 Quantification of nuclear and cytoplasmic ABCG2 staining in the glandular region of normal and malignant TMA prostate tissues. Immunohistochemical staining of ABCG2 was quantified in TMA group using the proportion and intensity 1 score for nuclear and cytoplasmic staining. (A) Nuclear ABCG2 staining showed no significant difference between normal and malignant prostate tissues (p= 0.9141). (B) Cytoplasmic ABCG2 staining was significantly decreased in PCa compared with NP tissues (p=<0.0001). (C) Nuclear ABCG2 nuclear staining was not associated with primary Gleason grade (p= 0.6933). (D) Cytoplasmic ABCG2 staining showed a significant difference among primary Gleason grades (p= 0.0004). Cytoplasmic ABCG2 staining was decreased in Gleason grade 5 compared to grade 4 (p= 0.0387) or grade 3 (p= 0.0003), and also a significant reduction when comparing between grade 4 and 3 (p= 0.0364). Unpaired or one-way ANOVA tests were conducted to determine the statistical difference for each set of conditions. NP (n=16), PCa (n=80), grade 3 (n=13), grade 4 (n=46) and grade 5 (n=18).

Table 2: Nuclear and cytoplasmic ABCG2 staining results with the Bath clinical data.

Comparison	Nuclear ABCG2 staining		Cytoplasmic ABCG2 staining	
	Results	p. value	Results	p. value
Normal vs malignant	No statistically significant difference	0.7873	Lower in malignant	0.048
Primary Gleason grades (3 & 4)	Higher in high grade	0.0221	No statistically significant difference	0.1199
Clinical Stage (T)	Higher in T3-4	0.0337	No statistically significant difference	0.327
5 years Biochemical recurrence	No statistically significant difference	0.8106	Lower in recurrence	0.0141

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Table 3: The Nuclear and cytoplasmic ABCG2 staining results with the TMA clinical data

Comparison	Nuclear ABCG2 staining			Cytoplasmic ABCG2 staining		
	Results		p. value	Results		p. value
Normal vs malignant	No statistically significant difference		0.9141	lower in malignant		< 0.0001
Primary Gleason grades (3, 4 & 5)	No statistically significant difference	Anova test	0.6933	lower in high Gleason grade	Anova test	0.0004
		Grade 4vs. Grade 3	0.978		Grade 4vs. Grade 3	0.0364
		Grade 5 vs. Grade 3	0.7393		Grade 5 vs. Grade 3	0.0003
		Grade 5 vs. Grade 4	0.7291		Grade 5 vs. Grade 4	0.0387
Stage (T)	No statistically significant difference		0.2507	No statistically significant difference		0.8698
Stage (M)	No statistically significant difference		0.398	No statistically significant difference		0.398
Stage (N)	No statistically significant difference		0.5885	No statistically significant difference		0.3307

Discussion

The major goal of this study was to identify a protein that is differentially expressed between normal and malignant prostate tissues and/or between different primary Gleason grades, clinical stages and recurrence vs non-recurrence PCa. This is important to improve our understanding of the molecular basis of PCa formation and progression and potentially help in the development of future biomarkers. To achieve this goal, the project involved evaluation of the expression of ABCG2 in prostate samples from two independent cohorts of patients using IHC.

This study found that cytoplasmic ABCG2 staining was reduced significantly in PCa compared to NP tissues. This data was supported by the literature (12) and taken together suggests that decreased cytoplasmic ABCG2 may play an important role in PCa formation. However, this data disagrees with the previous ABCG2 mRNA data that showed there was no significant association in ABCG2 mRNA level between normal and malignant using real-time PCR (9), suggesting there might be differences between mRNA and protein expression. It might also be that the difference is caused by using different methods for detection. In addition, this study reported that cytoplasmic ABCG2 staining was significantly reduced with increasing primary Gleason grade. This data is supported by Castellon *et al* data who reported that PCa tissues with a medium Gleason grade showed increased ABCG2 staining compared to those with a high Gleason grade (13). In addition, cytoplasmic ABCG2 staining was not associated with clinical stage, which is consistent with a previous finding on breast cancer (11). Data from the Bath cohort showed a significant reduction of cytoplasmic ABCG2 staining in relapsed tissues compared to those with non-relapsed, suggesting ABCG2 may play a role to prevent PCa relapse. This result is also contradictory with previous ABCG2 mRNA

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data (15). This might be because of the sample size and/ or using a different technique.

This study showed for the first time nuclear ABCG2 staining in prostate samples. The statistical analysis found no significant difference between nuclear ABCG2 staining when comparing NP tissues to those with malignancies. The Bath data shows that there was a positive association between nuclear ABCG2 staining and Gleason grade or clinical stage, but not with relapse. In contrast, the TMA data shows that nuclear ABCG2 was not associated with primary Gleason grade and clinical stage. ABCG2 as a transmembranous transporter protein is not expected to be expressed in the nuclei of cells, but two different studies have reported the nuclear localisation of ABCG2 in glioblastoma multiform cells (18) and lung cancer cells (19) using different IHC and immunofluorescence. This might suggest a role for ABCG2 in the nucleus, but another possibility is that the nuclear ABCG2 staining is non-specific.

Previous studies have proposed different roles for ABCG2 in human tissues, including cancer. The ABC transporter superfamily proteins use ATP hydrolysis to transport different molecules through the plasma membrane, including drugs (20). ABCG2 is found to play a role in transporting cytotoxic anti-cancer agents, as well as endogenous materials out of cells (21). A previous ABCG2 review reported that by active efflux of anticancer medicine, the expression of ABCG2 may directly cause multidrug resistance (22). However, ABCG2 may also play additional roles in promoting proliferation and maintaining the undifferentiated phenotype of SCs (10). A more recent study done by Sabnis *et al*. reported that ABCG2 has a role in the maintenance of prostate stem cells as well as in providing a rationale for targeting ABCG2 for differentiation therapy in PCa, using cancerous and non-cancerous prostate cell lines (23). This role might occur because inhibiting ABCG2-mediated androgen efflux with ABCG2 inhibitor (Ko143) increases the nuclear translocation of AR (23). A third study has identified that androgen-independent PCa patients with the Q141K variant have a shorter overall survival time than patients without the single nucleotide polymorphism (SNP) (24), suggesting that the reduced function of the variant ABCG2 protein helps to increase the intracellular concentration of androgen which may play a role in driving the proliferation of the cells. This last study appears most consistent with the loss of expression described here.

Data presented here suggest that downregulation of ABCG2 may play an important role in cancer formation and progression as well as increasing the risk of relapse. ABCG2 in the nucleus may have another role, but this role is still unclear. Further study is needed to confirm the nuclear localisation of ABCG2, perhaps using immunofluorescence or nuclear fractionation. In addition, it will very important to confirm ABCG2 staining in prostate tissues, using a second independent antibody (IHC) and/or mRNA probe (RNAscope®) in prostate sample from both cohorts. The future work could be carried out with an academic TMA cohort (25, 26& 27), which has clinical information about a risk of biochemical recurrence of PCa to assess the role of ABCG2 in a risk of recurrence. In addition, knockouts are perhaps the most robust method of validation and can help support the

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use of a particular antibody. This method can not be used in human tissues, but could be carried out in human cell lines that can then be embedded and used for IHC staining. Human knockout cell lines were generated by Horizon Company https://www.horizondiscovery.com/ for ABCG2 (HZGHC9429). This would improve the confidence that the staining patterns shown by IHC accurately reflect the expression of the protein.

In conclusion, decreased ABCG2 staining is observed in PCa and is negatively associated with Gleason grade and biochemical relapse. This preliminary data suggest that ABCG2 might play a role in PCa formation and progression and could be prognostic biomarkers for PCa. In addition, this work may represent an important step in improving understanding of the molecular basis of PCa formation and progression.

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انخفاض تعبير معلم (ABCG2) في سرطان البروستاتا وارتباطه سلبا مع مرحله التميز لخلايا سرطان البروستاتا والانتكاس

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الخلاصة

تم تحديد عدد قليل من المؤشرات الحيوية التنبؤية لسرطان البروستاتا، وهناك صعوبات إكلينيكية في التمييز بين الأمراض الانتكاسية وغير الانتكاسية. الهدف من هذه الدراسة هو التحقيق في الفرضية القائلة بأن ABCG2قد يكون علامة بيولوجية محتملة لسرطان البروستاتا ويمكن أن يميز بين الأورام العدوانية التي تتطلب تدخلات جذرية وتلك التي لديها تشخيص جيد .ABCG2 هو بروتين عبر الغشاء يلعب دورًا حيويًا في تعزيز التكاثر والحفاظ على النمط الظاهري غير المتمايز للخلايا الجذعية. يُعتقد أنه علامة بيولوجية محتملة يمكنها التنبؤ بالتقدم السريري والتشخيص لأنواع مختلفة من الأورام. ومع ذلك، لا يزال دوره في ورم البروستاتا غير واضح. تم تقييم التعبير النووي والهيولي (السايتوبلازمي) لمعلم (ABCG2) بطريقة التصبيغ المناعي النسيجي الكيميائي باستخدام مصدرين لعينات المرضى. تتكون مجموعة المصفوفة الصغيرة (TMA) من ٩٦ عينه بعضها طبيعي والأخر خبيث. ما مجموعه باث فمكونه من ٢٦ عينه، بما في ذلك عينات من مرضى يعانون من تكرار المرض او عدم تكراره. أظهرت الدراسة المناعية النسيجية تعبير معلم (ABCG2) في سايتوبلازم ونواه خلايا البروستات الطبيعية والسرطانية. كما أظهرت انخفاض التعبير السايتوبلازمي للمعلم في الأنسجة السرطانية مقارنة بالأنسجة الطبيعية للبروستاتا. وارتبط تعبير السايتوبلازمي للمعلم سلبا بزيادة درجه جليسون وكذلك الانتكاس في مجموعه باث. اضافه لوجود ارتباط سلبي بين تعبير المعلم. أظهرت هذه البيانات الأولية أن ABCG2 قد يلعب دورًا في تكوين السرطان و / أو العدوانية ويستدعي مزيدًا من التحقيق لفهم وظيفته وتحديد ما إذا كان يمكن أن يكون علامة بيولوجية تشخيصية محتملة لورم البروستاتا.

الكلمات المفتاحية: سرطان البروستاتا، المَعلمات، ABCG2، التصبيغ المناعي النسيجي الكيميائي.