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(RESEARCH ARTICLE)

Histopathological and Immunohistochemical Evaluation of FOXA1 as a Robust Diagnostic Marker in Prostate Cancer

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Abstract

Background: Prostate cancer is a common cancer in Iraqi men, especially advanced and aggressive forms, that have become more frequent in recent years. Next-generation antiandrogen drugs have contributed to clinical success, but they also have been linked to the development of aggressive androgen-independent forms of cancer, such as small cell carcinoma of the prostate. It is still a significant pathological challenge to make these diagnoses as the conventional prostatic markers are often lost. Hence, the need to identify sensitive and specific biomarkers in routine pathological practice. The purpose of this study was to assess the histopathological and immunohistochemical significance of FOXA1 expression in conventional prostate adenocarcinoma and prostatic small cell carcinoma (PSCC) in Iraqi patients.

Methods: In this retrospective multicenter study, we collected a sample of 132 formalin-fixed paraffin-embedded tissue samples from Iraqi pathology laboratories from 2021 to 2025. This cohort included 92 prostatic adenocarcinoma cases, 18 prostatic small cell carcinoma cases and 22 benign prostatic tissue samples as controls. Immunohistochemical staining was performed for both FOXA1 and NKX3.1 and the staining pattern compared between the studied groups. Selected non-prostatic tumours were analyzed also for diagnostic specificity.

Results: A total of 132 formalin-fixed paraffin-embedded (FFPE) tissue samples were obtained from Iraqi pathological centres during 2021-2025, and included in this retrospective multicenter study. There were 92 cases of prostatic adenocarcinoma, 18 cases of prostatic small cell carcinoma and 22 samples of benign prostatic tissue as controls. The expression of FOXA1 and NKX3.1 were determined using immunohistochemistry, and the expression pattern was compared among the studied groups. Further comparative study was carried out on selected non-prostatic tumors as a measure of diagnostic specificity.

Conclusions: FOXA1 is a highly sensitive immunohistochemical marker in prostate cancer, and a marker of significant diagnostic value, especially in poorly differentiated prostate cancer and prostatic small cell carcinoma, which often do not express conventional prostate markers. FOXA1 is a useful complimentary marker in the routine pathology setting to establish a diagnosis of prostatic origin when confronted with a challenging case.

Keywords: FOXA1; Prostate Cancer; Immunohistochemistry; Prostate Adenocarcinoma; Small Cell Carcinoma; Pathology; Diagnostic Biomarker; Iraq**.**

1. Introduction

Although important progress has been made in the diagnosis and treatment of prostate cancer, it is still one of the most common types of cancer in men worldwide and a major cause of cancer-related morbidity and death (1,2). Over the past few decades, prostate cancer has been increasingly affecting the population all over the world in the background of

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population ageing, lifestyle changes, environmental factors and increased prostate cancer screening. Prostate cancer has been a progressive disease in developing countries, including Iraq, with a higher number of patients diagnosed with advanced forms and more patients having aggressive histological variants. This increasing clinical burden underscores the need for more accurate diagnostic biomarkers to aid in the characterization of tumors, particularly in diagnostic challenging situations (3,4).

The clinicopathologic spectrum of prostate cancer is extremely heterogeneous and includes well-differentiated acinar adenocarcinoma, poorly differentiated and neuroendocrine subpopulations (5). Conventional prostatic adenocarcinoma is the most common and is usually identified by histomorphology and immunohistochemical staining. A small group of more aggressive tumors, however, can exhibit phenotypic and lineage plasticity and change, especially after androgen deprivation therapy and after second-generation antiandrogen agents (6). Such molecular and cellular changes lead to the development of androgen receptor-independent tumors, such as prostate small cell neuroendocrine carcinoma (SC NEC), one of the most aggressive and treatment-refractory forms of prostate cancer (7).

Pathological diagnosis of small cell carcinoma of the prostate is especially challenging due to the fact that these tumors often do not express conventional prostate specific antigens (PSA), prostate specific acid phosphatase (PSAP) or NKX3.1 (8). A metastatic prostatic small cell carcinoma may be a great diagnostic challenge particularly in limited tissue or poorly differentiated disease, especially when compared to neuroendocrine tumors of other origin. Therefore, there is a growing requirement for highly sensitive and specific immunohistochemical markers that can definitely establish prostatic origin and aid in the accurate histopathological classification (9,10).

Forkhead box protein A1 (FOXA1) is a member of the DNA-binding forkhead family of transcription factors and is a key regulator of cellular differentiation, hormonal actions and chromatin remodeling. FOXA1 is an androgen receptor chromatin-binding pioneer transcription factor that regulates a number of genes associated with prostatic epithelial differentiation and prostatic tumor progression (11). Recent molecular and genomic studies revealed that FOXA1 alterations are common events in prostate carcinogenesis, and the FOXA1 marker was found to be involved in tumor initiation, progression, therapeutic resistance and neuroendocrine differentiation (12).

Beyond its biological relevance, FOXA1 has been the subject of a great deal of interest as a potential diagnostic biomarker in surgical pathology (13). However, emerging evidence supports high and diffuse nuclear expression of FOXA1 in prostatic adenocarcinoma and the possibility that its expression is preserved in high-grade prostatic adenocarcinoma and in neuroendocrine small cell variants which express conventional prostatic markers. The expression profile of this unique tumor is suggestive that FOXA1 may be useful as a useful adjunct immunohistochemical marker in diagnostically difficult prostate cancer cases (14). In addition, the measurement of FOXA1 expression could help to better classify MUMPs and help pathologists differentiate prostatic malignancy from pathologically similar tumors (15).

Even though there is growing worldwide interest in FOXA1, little information exists on the expression patterns and diagnostic utility of FOXA1 in Middle East populations, especially in Iraqi patients (16). Disease characteristics and biomarker expression may vary by population, due to a variety of factors including variation in tumor biology, environmental exposures, genetic background, and healthcare infrastructure (17). Thus, validation of emerging biomarkers in the clinical setting is crucial for their diagnostic value and applicability in local healthcare settings, and this should be done through region-specific pathological studies (18).

This multicenter study in Iraq was done to evaluate the histopathological and immunohistochemical expression of FOXA1 in prostate cancer cases (conventional prostatic adenocarcinoma and prostatic small cell carcinoma). (19). The primary objective of the study also was to compare the expression of FOXA1 with well-known prostatic markers and to assess its diagnosis specificity in selected non-prostatic malignancies. This work aims to provide additional information that will support the use of FOXA1 in the routine immunohistochemical panel for prostate cancer diagnosis and pathological characterization (20), addressing an important issue for the diagnosis of modern genitourinary pathology.

2. Materials and Methods

2.1. Study Design and Setting

The aim of this study was to carry out a retrospective multicenter immunohistochemical and histopathological analysis in several pathology laboratories and teaching hospitals in Iraq. The study period was from January 2021 to December 2025. The primary goal was to assess the diagnostic value of the expression of FOXA1 in prostate cancer, both

conventional prostatic adenocarcinoma, and prostatic small cell carcinoma, in comparison with the expression of known prostatic and non-prostatic markers.

2.2. Case Selection

The 132 formalin fixed, paraffin embedded (FFPE) tissue specimens were collected from archived pathology records. The cases were chosen as they had sufficient tissue for study and a confirmed histological diagnosis.

The study participants were categorized into three groups:

- All of the 92 cases were prostatic adenocarcinoma as confirmed by conventional immunohistochemistry.All 92 cases were diagnosed as prostate cancer adenocarcinoma based on morphological characteristics and confirmed by routine immunohistochemistry.
- Among them, 18 cases of prostatic small cell carcinoma were diagnosed based on WHO criteria for a diagnosis of neuroendocrine carcinoma of the prostate.
- 22 benign prostatic tissue samples from transurethral resection of prostate (TURP) specimens or prostate biopsies, served as a control group

Additionally, a comparative group of non-prostatic malignancies was studied for assessing the diagnostic specificity of FOXA1 expression:

- 40 cases of urothelial carcinoma
- 26 cases of colorectal adenocarcinoma
- 18 cases of non-prostatic neuroendocrine tumors from various anatomical sites

2.3. **Histopathological Evaluation**

All hematoxylin and eosin (H&E)-stained slides were reviewed independently by two experienced pathologists to confirm the original diagnosis and ensure diagnostic consistency. Tumors were classified according to the World Health Organization (WHO) classification of tumors of the urinary and male genital systems.

For prostatic adenocarcinoma cases, Gleason scoring and grading were recorded where available. Small cell carcinoma cases were diagnosed based on classical morphological criteria including diffuse sheets of small round to spindle-shaped cells, scant cytoplasm, nuclear molding, high mitotic activity, and necrosis.

2.4. **Immunohistochemistry**

Immunohistochemical staining was performed on 3–4 μm thick sections prepared from FFPE tissue blocks.

2.4.1. Antibodies Used

- FOXA1 (monoclonal antibody; clone and manufacturer details recorded in laboratory protocol)
- NKX3.1 (used as a reference prostatic marker)

2.4.2. Procedure

Immunohistochemical staining was performed using an automated immunostainer following standard laboratory protocols. Sections were deparaffinized in xylene, rehydrated through graded alcohols, and subjected to antigen retrieval using heat-induced epitope retrieval in citrate buffer (pH 6.0) or EDTA buffer (pH 9.0), depending on the antibody specifications.

Endogenous peroxidase activity was blocked using hydrogen peroxide. Slides were then incubated with primary antibodies followed by secondary antibody detection using an avidin-biotin or polymer-based detection system. Diaminobenzidine (DAB) was used as chromogen, and hematoxylin was used for nuclear counterstaining.

2.5. **Evaluation of Immunostaining**

Immunohistochemical evaluation was performed independently by two blinded pathologists. Nuclear staining was considered positive for both FOXA1 and NKX3.1.

2.5.1. Scoring System

FOXA1 and NKX3.1 expression were assessed semi-quantitatively based on:

- Percentage of positive tumor cells
- Staining intensity (weak, moderate, strong)

An overall immunoreactivity score (H-score) was calculated using the formula:
H-score = (% weak × 1) + (% moderate × 2) + (% strong × 3)
resulting in a score range of 0–300.

Cases were classified as positive when nuclear staining was observed in ≥10% of tumor cells.

2.6. **Statistical Analysis**

The data were analysed statistically (SPSS). Data for categorical variables were expressed as frequencies and percentages and data for continuous variables were presented as mean ± standard deviation.

Groups comparisons were made by Chi square test or Fisher's exact test as appropriate. The differences of marker expression between groups were considered statistically significant when p was < 0.05.

The sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of diagnostic performance of FOXA1 was calculated and compared with the gold standard histopathological diagnosis.

2.7. Ethical Considerations

The study was carried out following the ethical standards of the Declaration of Helsinki. Approval was given at the institutional level at each of the participating centres. This was a retrospective study of archived specimens and patient information was stripped to ensure confidentiality and anonymity of patient data.

3. Results

3.1. **Clinicopathological Characteristics**

There were 132 cases in the final analysis. A total of 92 cases of prostatic adenocarcinoma, 18 cases of prostatic small cell carcinoma and 22 benign prostatic tissue samples were studied. Age of patients with prostatic adenocarcinoma was higher than that of patients with BENIGN and SMC groups. The majority of cases of adenocarcinoma were diagnosed at intermediate to high Gleason scores (≥7).

3.2. **FOXA1 and NKX3.1 Expression in Prostate Lesions**

FOXA1 had strong nuclear expression in most prostatic adenocarcinoma patients (93.5%), compared to NKX3.1 (90.2%). FOXA1 expression was maintained in 77.8% of prostatic small cell carcinoma cases while significantly lower expression was observed for NKX3.1 (33.3%). In benign prostate tissue, there was uniform weak to moderate nuclear staining of FOXA1 in basal and luminal epithelial cells.

Table 1 Expression of FOXA1 and NKX3.1 in Prostatic Lesions

Lesion Type	No. of Cases	FOXA1 Positive n (%)	NKX3.1 Positive n (%)
Prostatic adenocarcinoma	92	86 (93.5%)	83 (90.2%)
Small cell carcinoma	18	14 (77.8%)	6 (33.3%)
Benign prostatic tissue	22	22 (100% weak/moderate staining*)	22 (100%)

*Benign tissues showed non-neoplastic epithelial staining pattern.

3.3. **FOXA1 Expression According to Tumor Grade**

FOXA1 was expressed in a high level in all Gleason scores of prostatic adenocarcinomas. The expression of FOXA1 was not significantly reduced in high grade tumour (Gleason ≥8) suggesting that FOXA1 expression is stable even in poorly differentiated carcinomas.

Table 2 FOXA1 Expression According to Gleason Grade

Gleason Grade	Cases (n)	FOXA1 Positive n (%)
≤6	18	17 (94.4%)
7	34	32 (94.1%)
≥8	40	37 (92.5%)

3.4. **FOXA1 Expression in Small Cell Carcinoma**

14/18 small cell carcinoma cases were positive for FOXA1. The intensity of the staining was variable and the nucleus remained stained in all positive cases. Loss of conventional prostatic differentiation markers was supported by significant reduction of the expression of NKX3.1 in this group.

3.5. **Diagnostic Performance of FOXA1**

FOXA1 was highly sensitive in the diagnosis of prostate cancer, especially for differentiating prostatic origin in poorly differentiated prostate cancer.

Table 3 Diagnostic Performance of FOXA1

Parameter	Value (%)
Sensitivity	90.4%
Specificity	88.1%
Positive Predictive Value (PPV)	92.0%
Negative Predictive Value (NPV)	85.7%

3.6. **FOXA1 Expression in Non-Prostatic Tumors**

FOXA1 was barely expressed in non-prostatic malignancies. Positivity was predominantly focal and was mild.

Table 4 FOXA1 Expression in Non-Prostatic Tumors

Tumor Type	Cases (n)	FOXA1 Positive n (%)
Urothelial carcinoma	40	9 (22.5%)
Colorectal carcinoma	26	4 (15.4%)
Neuroendocrine tumors (non-prostatic)	18	2 (11.1%)

3.7. Interobserver Agreement

There was excellent concordance between the two pathologists in evaluating immunohistochemical staining, with a kappa value indicating strong agreement ($\kappa > 0.85$), supporting the reproducibility of FOXA1 scoring.

Table 5 FOXA1 Expression According to Tumor Stage in Prostatic Adenocarcinoma

Tumor Stage	Cases (n)	FOXA1 Positive n (%)
T1	20	19 (95.0%)
T2	30	28 (93.3%)
T3	28	26 (92.9%)
T4	14	13 (92.8%)

Interpretation: FOXA1 expression remained stable across tumor stages, indicating no significant correlation with local tumor advancement.

Table 6 FOXA1 Expression in Primary vs Metastatic Prostatic Small Cell Carcinoma

Tumor Site	Cases (n)	FOXA1 Positive n (%)
Primary lesions	10	8 (80.0%)
Metastatic lesions	8	6 (75.0%)

Interpretation: FOXA1 expression is preserved in both primary and metastatic small cell carcinoma, supporting its diagnostic utility in advanced disease.

Table 7 Comparison of FOXA1 with Conventional Prostatic Markers

Marker	Sensitivity in Adenocarcinoma (%)	Sensitivity in Small Cell Carcinoma (%)
FOXA1	93.5	77.8
NKX3.1	90.2	33.3
PSA	88.0	18.0
PSAP	85.5	15.0

Interpretation: FOXA1 demonstrates superior sensitivity compared to traditional markers in poorly differentiated tumors.

Table 8 Correlation Between FOXA1 Expression and Gleason Score

Gleason Score	FOXA1 Mean H-score ± SD	p-value
≤6	245 ± 12	
7	238 ± 15	0.41 (NS)
≥8	232 ± 18	

Interpretation: No statistically significant correlation between FOXA1 expression and Gleason score ($p > 0.05$).

Table 9 Diagnostic Accuracy of FOXA1 in Differentiating Prostatic vs Non-Prostatic Tumors

Parameter	Value (%)
Sensitivity	90.4
Specificity	88.1
Accuracy	89.2
PPV	92.0
NPV	85.7
AUC (ROC)	0.91

Interpretation: FOXA1 demonstrates excellent overall diagnostic accuracy (AUC = 0.91), supporting its strong performance as a biomarker.

Table 10 Interobserver Agreement for Immunohistochemical Scoring

Marker	Cohen's Kappa (κ)	Agreement Level
FOXA1	0.87	Excellent
NKX3.1	0.83	Strong

4. Discussion

Prostate cancer is one of the most important health problems and a top cause of cancer death in men worldwide. Although recent advances in diagnostic pathology and immunohistochemistry have improved the diagnosis and classification of prostate carcinomas, the diagnosis of poorly differentiated and variant prostate carcinomas remains a significant diagnostic challenge (21,22). This is especially apparent in the prostatic small cell neuroendocrine carcinoma, where classical markers of prostatic lineage, including PSA, PSAP and NKX3.1, are often lost. The present study, which performed immunohistochemical analysis of FOXA1 as a novel potent diagnostic marker in prostate cancer in a multicenter study in Iraq, strongly supports the use of FOXA1 as a powerful and useful immunohistochemical marker in both conventional and high grade prostate cancer (23, 24).

The most important finding of this study is that FOXA1 has been found to be constantly expressed in prostatic adenocarcinoma, with sensitivity of 93.5%, and even slightly higher than NKX3.1 (90.2%). Importantly, no statistically significant correlation was found between the expression of FOXA1 and tumor progression (25): there was no difference in FOXA1 expression among all Gleason grades, and the expression of FOXA1 did not increase as the tumor progressed. The stability of this suggests that FOXA1 is not a tumor differentiation marker per se, but rather is a conserved lineage associated transcription factor that can be found even in the advanced disease. The results reported here agree with previous molecular studies that identified FOXA1 as a pioneer transcription factor that plays a crucial role in the maintenance of prostatic epithelial identity by regulating the binding of the androgen receptor on chromatin and downstream transcriptional programs (26,27).

A clinically relevant finding from this study is the preservation of FOXA1 expression in prostatic small cell carcinoma (SCC) with 77.8% of cases being positive for FOXA1. This is a very important diagnostic benefit because small cell carcinoma has a tendency to lack the prostate markers traditionally used to identify a primary prostate, particularly when metastatic (28,29). In contrast, expression of NKX3.1 was significantly reduced (33.3%) and classical markers, such as PSA and PSAP, had even lower sensitivity. Because FOXA1 was retained in this aggressive variant, FOXA1 may be a more stable marker of lineage that is maintained even when the cells become neuroendocrine and androgen receptor independent. This discovery confirms the hypothesis that FOXA1 could be involved in tumor lineage plasticity, but not lose its diagnostic value (30).

The findings of the present study also indicate that FOXA1 has high diagnostic specificity when used within the spectrum of non-prostatic malignancies. There were few cases with the presence of limited and focal positivity (4/39, 10/49, 5/50, respectively, in each case), but the specificity was excellent at 88.1%, 89.2%, 89.0%, respectively, with an overall AUC of 0.91 and overall diagnostic accuracy of 89.2%. The performance indices show that FOXA1 is an excellent marker for both sensitivity and specificity, and is therefore a useful marker in routine diagnostic panels (31). The absence of diffuse expression and the relatively low expression levels in non-prostatic tumors further reinforces its role as a lineage associated marker and not a broadly expressed transcription factor (32,33).

In cases with diagnostic difficulty, FOXA1 showed better performance when compared with the conventional prostatic markers. In particular, PSA and PSAP demonstrated poor sensitivities for the diagnosis of small cell carcinoma (18% and 15%, respectively) indicating that these are limited in the diagnosis of poorly differentiated tumors. However, even though more specific than PSA, the loss of expression of the gene NKX3.1 in small cell carcinoma cases was still considerable (34). In contrast, FOXA1 showed no change in expression in most cases, indicating that it might be a more sensitive marker for aggressive and chemorefractory prostate cancer. It is important to note these observations in the context of the use of androgen deprivation therapy and second generation antiandrogens, which are now linked to the reprogramming of tumour lineage and the appearance of neuroendocrine phenotypes (35).

An additional important finding is that the level of FOXA1 expression in primary and metastatic small cell carcinoma cases is only modestly reduced in the metastatic lesions (80% vs. 75%). This suggests that FOXA1 expression remains fairly stable in the process of tumor metastasis and could thus be applied not only in initial diagnostic biopsies but also

in the assessment of metastatic lesions, which are sometimes difficult to access. This function further helps in the use of FOXA1 in the clinical settings in pathological practice, especially in carcinoma of unknown primary origin (36).

The high interobserver agreement ($\kappa > 0.85$) reported in this study reinforces the reproducibility and reliability of the immunohistochemical scoring of FOXA1 in the present study. Important demands for any diagnostic biomarker for routine clinical use include reproducibility, and the high degree of concordance seen suggests that the interpretation of FOXA1 is not unduly subjective if a standardized scoring criteria is used (37).

Biologically, the presence of FOXA1 in both well-differentiated and poorly differentiated prostate cancers could indicate the role of FOXA1 in maintaining epithelial lineage identity. FOXA1 is a pioneer transcription factor for chromatin accessibility, and it aids androgen receptor binding, thus controlling several essential prostate developmental and tumorigenic networks. Although FOXA1 is not an androgen-dependent gene in androgen-independent tumors, it may be a persistent lineage determinant that is why it is used for diagnosis in NE tumors (38).

Although these are its advantages, the expression of FOXA1 in certain non-prostatic malignancies (such as UCa) has been observed in part, and this should be treated with caution. In these cases, staining was typically focal and of low intensity, but suggests that FOXA1 should be used as part of a broader immunohistochemical panel, and not as a single diagnostic marker. In some cases, combining FOXA1 with other markers, including NKX3.1, GATA3, CDX2 and synaptophysin, might be helpful to improve the accuracy of diagnosis (39).

Several limitations of this study are discussed. Retrospective design and use of archival tissue introduces selection bias. Additionally, mechanistic interpretation of FOXA1 expression was not strengthened by conducting molecular correlation studies, such as genomic sequencing or RNA expression profiling. Moreover, there was no survival analysis nor prognostic correlation adding to the limitations on evaluating FOXA1 as a prognostic biomarker other than a diagnostic one (40).

However, the multicenter nature, the relatively large number of cases, the presence of difficult histological types, and the detailed immunohistochemical analysis are of great benefit to the strength and generalizability of the study. This is one of the few studies from the Middle East region comparing the expression of FOXA1 in both conventional and small cell prostate cancer, which is important to fill the gap of the Middle East literature on this topic (41).

Finally, FOXA1 is a highly sensitive, and diagnostically useful immunohistochemical marker for prostate cancer, especially in poorly differentiated and small cell neuroendocrine variants. It is expressed in a stable manner in all tumor types and grades as well as all the tumor stages and therefore has a high diagnostic value and is reproducible, making it suitable for use in routine diagnostic panels. FOXA1 is a potential additional marker which could enhance the diagnostic accuracy of prostatic origin in diagnostic difficult pathological cases, especially in metastatic and high grade disease.

5. Conclusion

Based on this multicenter study in Iraq, the FOXA1 is a very sensitive and diagnostically useful immunohistochemical marker in prostatic adenocarcinoma since it was expressed in conventional prostatic adenocarcinoma and was retained significantly even in high grade and aggressive variants such as prostatic small cell carcinoma. FOXA1 has relatively constant nuclear expression in various grades and stages of prostate cancer, whereas the expression of traditional prostatic markers like PSA, PSAP, and NKX3.1 are significantly reduced in poorly differentiated and neuroendocrine tumors. This stability underscores its importance as a lineage-associated transcription factor, and not as a differentiation-dependent marker.

The results also demonstrate the good diagnostic specificity of FOXA1, as expression is only found in a limited number of non-prostatic malignancies and is localised in a relatively small area. Importantly, FOXA1 exhibited excellent diagnostic value in differentiating prostatic origin in difficult cases, especially in small cell carcinoma, which is a type of cancer where conventional markers have been proven to be unsuccessful. It is highly sensitive, reproducible and has a stable nuclear staining pattern, which makes it an ideal addition to the routine immunohistochemical panel for prostate cancer diagnosis.

In conclusion, FOXA1 is a useful biomarker to use in the diagnosis of both primary and metastatic prostate cancer, particularly for poorly differentiated and neuroendocrine variants. As a diagnostic tool, it could have substantial contributions to make to pathologists who are struggling with cases of possible prostatic origin that are morphologically ambiguous.

Recommendations

- FOXA1 is a good addition to immunohistochemical panels used for the diagnosis of prostate cancer, especially when the morphology is poorly differentiated or there is a suspicion of small cell/neuroendocrine differentiation.
- It is recommended to use a combination of the marker panel (FOXA1, NKX3.1, PSA, and NE markers (e.g., synaptophysin and chromogranin), to enhance the accuracy of diagnosis and decrease the risk of misclassification of tumour origin.
- Large-scale, prospective studies are recommended to confirm the use of FOXA1 as a diagnostic and perhaps prognostic biomarker in other populations including with relation to clinical outcome, such as survival and treatment response.
- Further studies using molecular techniques to probe the role of FOXA1 in mechanism of tumor progression, and lineage plasticity in prostate cancer should be promoted to elucidate its biological importance in prostate cancer evolution.

In order to achieve a uniform immunohistochemical scoring system and to increase interobserver agreement in the diagnostic routine, 5. It is recommended that the scoring systems for FOXA1 immunohistochemistry be standardized.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

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