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SMARCC1 expression is upregulated in prostate cancer and positively correlated with tumour recurrence and dedifferentiation

S. Heebøll[1,2,3], M. Borre[2], P.D. Ottosen[3], C.L. Andersen[1], F. Mansilla[1], L. Dyrskjøt[1], T.F. Ørntoft[1] and N. Tørring[1]

[1]Molecular Diagnostic Laboratory, Department of Clinical Biochemistry, Aarhus University Hospital - Skejby, [2]Department of Urology, Aarhus University Hospital, Skejby and [3]Department of Pathology, Aarhus University Hospital, Aarhus, Denmark

Summary. Background. The identification of new prognostic markers in prostate cancer (PC) is essential to improve patient treatment and management. Data suggest that SMARCC1 protein, a part of the intranuclear SWI/SNF complex which enhances the transactivation of the androgen receptor, is upregulated in PC and therefore a possible candidate marker for PC progression. Materials. Expression of SMARCC1 immunostaining was analysed on a tissue microarray containing specimens from 327 patients with prostate cancer and clinical follow-up information. Furthermore, 30 specimens from patients with benign prostate hyperplasia were included as controls as well as 30 specimens of benign prostate tissue from PC patients. Also, 18 specimens from lymph node metastases were analysed. Results. All benign specimens showed no or minimal staining for SMARCC1. In contrast, 20% of the specimens from patients with non-metastatic and non-recurrent disease showed moderate to marked staining. In 31% of the patients with recurrent disease and in 31% of the patients with metastatic disease we found moderate to strong SMARCC1 immunostaining. In total, 23% of lymph node metastases expressed SMARCC1. SMARCC1 expression was also positively correlated to Gleason score ($p<0.05$), clinical T stage ($p<0.01$) and time to recurrence ($p<0.001$). In a logistic regression analysis, patients with a marked SMARCC1 immunostaining had a significantly elevated odds ratio (OR) of 16 for recurrent cancer and an OR of 4.5 for metastatic disease. Conclusions. Our present results demonstrate an increased expression of SMARCC1 protein in prostate cancer and reveal a positive correlation with tumour dedifferentiation, progression, metastasis and time to recurrence.

Key words: Prostate cancer, SMARCC1, BAF155, Rissue microarray, Androgen receptor

Offprint requests to: Niels Tørring, Molecular Diagnostic Laboratory, Department of Clinical Biochemistry, Aarhus University Hospital - Skejby, Brenstrupgårdsvej 100, DK-8200 Aarhus N, Denmark. e-mail: nto@ki.au.dk

Introduction

Due to marked genetic and biological heterogeneity, the clinical course of prostate cancer (PC) is highly variable (reviewed by Eder et al., 2004). Currently, clinicians cannot discriminate between latent and aggressive prostate cancer at an early stage of disease. Patient stratification is therefore insufficient, leading to over-treatment, unnecessary morbidity and suffering to some, as well as under-treatment, unnecessary suffering and death to others. Hence, there is an urgent need for new diagnostic procedures in order to improve patient stratification, thereby allowing individualised clinical handling and treatment of PC patients. A better understanding of the biology underlying tumour latency, recurrence and metastasis is an essential prerequisite for future improvement of the prediction, prevention and treatment of prostate cancer.

The SMARCC1 (BAF155) gene product is part of the intranuclear SWI/SNF complex, which is a major complex of ATP-dependent chromatin remodelling factors. These factors contribute to the regulation of gene expression by altering chromatin structure (reviewed by Roberts and Orkin, 2004). The SWI/SNF complex is implicated in the modulation and transactivation of several nuclear receptors, including the androgen receptor (AR) (Inoue et al., 2002; Huang et al., 2003; Marshall et al., 2003; Hong et al., 2005; Link et al., 2005). Furthermore, hormone-dependent activation of AR seems partly dependent on SWI/SNF

action (Huang et al., 2003; Marshall et al., 2003). An alternative function of SMARCC1 has been suggested by Hong et al. (2005), who found that the mouse homolog Srg3 enhances transactivation of the androgen receptor in a seemingly SWI/SNF-independent manner. Together, these findings indicate that SMARCC1 may play a direct role in prostate cancer development and/or progression, since it is well-known that PC proliferation and survival depend on androgen receptor activity (reviewed by Agoulnik and Weigel, 2006).

The SMARCC1gene is located in a genomic region at chromosome 3p21-p23 (Ring et al., 1998), which we previously have found amplified in approximately 20% of samples of prostate cancer by high resolution SNP array in laser microdissected prostate tumour tissue (Tørring et al., 2007). Other prostate gene expression profiling studies have identified SMARCC1 as over-expressed in PC (Lapointe et al., 2004; Varambally et al., 2005; Tomlins et al., 2007).

In the present study, we have investigated the significance of SMARCC1 protein expression in PC development and progression, using immunohisto-chemistry on a large PC tissue microarray (TMA) with matching clinical, pathological and follow-up information. We found that SMARCC1 protein expression is significantly up-regulated in PC cancer as opposed to benign prostate tissue, and furthermore, correlates positively with Gleason score, tumour stage and time to recurrence.

Material and methods

Patients and tissues

A total of 287 PC patients who were treated for clinically localized PC by intended radical prostatectomy at the Department of Urology, Aarhus University Hospital – Skejby, from 1998 through 2005 were included in this study. Moreover, 40 patients treated for generally non-localized PC by transurethral resection of the prostate from 1992 to 1996 or from 1999 to 2005 were included. As control patients, tissue from 30 patients with benign prostate hyperplasia (BPH) and benign tissue from 30 patients with prostate cancer were included. Specimens from 18 lymph node metastases were also included in the PC tissue microarray, as well as high grade prostate intraepithelial neoplasia (PIN) tissue from 15 patients with PC. Presence of high grade PIN was confirmed by simultaneous basal cell cytokeratin/racemase staining on donor blocks. Cases were selected based on diagnosis and the quality and quantity of the available tissue on the paraffin block.

Clinico-pathological, follow-up and survival data were available for all patients. Clinico-pathological data included e.g. age and serum PSA at diagnosis, clinical and pathological TMN stage (UICC 2002), Gleason score and information on tumour volume and patient treatment. Follow-up data were available for all PC patients and included time to recurrence and/or time to death with a median follow-up time of 28 months (range 6-151 months). The study was approved by the local ethical committee.

Tissue microarray construction

The prostate TMA was constructed as described elsewhere (Bubendorf, 2001). In brief, the most representative tumour areas were carefully selected and marked based on the matched hematoxylin-eosin-stained slides. Altogether, 420 cores (diameter 0.6mm) of test tissue were taken from the donor blocks with the tissue microarrayer (Beecher Instruments, Silver Spring, MD, USA) and inserted into one of three recipient blocks; 159 cores of test tissue were inserted in Block 1, 151 in Block 2 and 110 in Block 3. The three blocks contained a mixture of tissue so that both benign and malign tissue of different Gleason grades and outcomes are represented on each block.

Sections of 3 μm were cut on a microtome and transferred to glass slides (Menzel-Gläser, SuperFrost®Plus, Germany) in the usual manner. The presence of tumour tissue was verified on a haematoxylin-eosin stained section and a basal cell cytokeratin staining (monoclonal mouse anti-human Cytokeratin HMW, 1:50, DakoCytomation, Denmark).

Immunohistochemistry

Sections were deparaffinized in ethanol and rehydrated by water rinses. Endogenous peroxidase activity was blocked (0.6% H_2O_2 in TBS buffer). Antigen retrieval was performed by treatment in a microwave oven (350V) in TEG buffer (pH 9, Tris Base 10 mM, EGTA 0.5 mM, demineralized water, Bie & Berntsen, Denmark). Non-specific binding was blocked by 1% bovine serum albumin (Albumin – Fraction V, Applichem, Germany) in TBS buffer. Sections were stained with the monoclonal mouse anti-SMARCC1 antibody (1:250, sc-32763 (DXD7), Santa Cruz Technologies, CA, USA) and with monoclonal goat anti-mouse antibody (EnVision+® System Labelled Polymer-HRP, K4001, DakoCytomation, Denmark). The primary antibody was omitted for negative controls. Slides were then incubated with 3.3'-diaminobenzidine chromogen (DakoCytomation, DK), counterstained in haematoxylin and mounted for microscopy.

All sections were scored, blinded and independently, by a clinical pathologist and a person with considerable training in histopathological scoring. Signals were considered positive when reaction products were localized in the expected cellular compartment. The staining showed an 'all-stain' or 'no-stain' pattern in the individual samples, and therefore, intensity rather than relative number of stained cells was scored. The intensity of the signal was scored as 0 (no staining, Fig. 2A), 1 (weak staining, Fig. 2B), 2 (moderate staining, Fig. 2C) and 3 (marked staining, Fig. 2D). Cases of divergence were solved by reviewing the samples

together and then coming to an agreement. Lost specimens or specimens with questionable signals due to insufficient tumour cells or tissues with homogeneous weak signals were excluded from further evaluation.

Cell culture, transfection, plasmids and Western blotting

To determine the sensitivity and specificity of the SMARCC1 antibody, we performed Western blot analysis on transfected cell cultures. Also, the development, specificity and sensitivity of the antibody have been described by Wang et al., 2005.

COS7 cells cultured in RPMI 1640 medium supplemented with 10% FCS and 1% penicillin-streptomycin at 37°C and 5% CO_2 were transfected with pcDNA3.1/V5-His:SMARCC1 (kind gift from Trevor Archer (Chen and Archer, 2005)) or pcDNA3.1/V5-His (mock) (Invitrogen, CA, USA), using Lipofectamine (Invitrogen) following the manufacturer's instructions. Cells were harvested and lysed in lysis buffer (50 mM Tris.HCl pH 8.0, 150 mM NaCl, 1 mM DTT, 1% Triton X-100, and protease inhibitor ROCHE complete, EDTA free). Twenty to thirty μg total protein samples were run in 12% SDS gels (Invitrogen) and transferred to nitrocellulose membranes. Membranes were blocked with 3% w/v non-fat powder milk PBS. The primary antibody was either mouse-anti-V5 (1:3000, Abcam Ltd, UK), mouse anti-SMARCC1 (1:500, sc-32763 (DXD7), Santa Cruz Technologies, CA, USA) or mouse anti-beta-actin (1:1000, Sigma-Aldrich, Germany. The secondary antibody was goat anti-mouse HRP conjugated (1:5000, EnVision+® System, DakoCytomation, DK). The immunoreactive bands were visualised using ECL plus (Amersham Biosciences, NJ, USA) and a UVP ChemiDoc-It, Imaging system, (UVP Inc., CA, USA).

Statistics

Comparison of clinico-pathological factors and SMARCC1 expression was performed using the χ^2 test, Kendall's π and a logistic regression test. Spearman's rank correlation was used to compare the serum PSA level at diagnosis and SMARCC1 expression. Time to recurrence curves were plotted according to Kaplan-Meier, and a log rank test and Cox proportional hazard regression analysis was used to compare recurrence curves between groups. The levels of statistical significance were set at $p<0.05$ (two-sided) and p values are generally indicated as $p<0.05$, $p<0.01$, $p<0.005$ or $p<0.001$. Statistical calculations were performed using SPSS for Windows (version 13.0, Chicago, Il, USA) and Stata (version 10, Texas, USA).

Results

Antibody specificity

Initially, we investigated the specificity of the monoclonal SMARCC1 antibody by Western blotting analysis using COS7 cells transfected with pcDNA3.1:SMARCC1:V5-His or a mock vector (Fig. 1). Anti-V5 antibody and anti-SMARCC1 identified two primary, identical bands of approximately 100 and 150 kDa (123 kDa is the predicted size of full-length SMARCC1) in the cells extracts overexpressing the tagged protein.

Tissue microarray and immunohistochemistry

To characterize the expression pattern of SMARCC1 protein in non-malignant prostate and prostate cancer, a tissue microarray was generated and stained with the monoclonal SMARCC1 antibody. The TMA cohort comprised prostate tissue samples from 327 patients with prostate cancer, 30 patients with benign prostate hyperplasia, 15 with high grade PIN and 18 specimens from lymph node metastases. Clinico-pathological descriptors of PC patients are displayed in Table 1.

In all positive cases, immunostaining for SMARCC1 was localized in the nucleus of cells with merely discrete staining of the cytoplasm (Fig. 2). Only 11 specimens were missing or not fit for evaluation due to low quality of sectioning or staining.

There was no or only weak immunostaining for SMARCC1 in all benign specimens from patients with BPH or PC, whereas two of 15 (13%) specimens from high grade PIN patient showed a marked immunoreaction. The difference in SMARCC1 expression in benign prostate specimens versus high grade PIN specimens was highly significant ($p<0.005$), though based on a small patient population.

Furthermore, 24% of the PC specimens investigated showed moderate to marked immunostaining, clearly showing that SMARCC1 immunostaining was significantly elevated in carcinoma specimens compared with benign prostate tissue ($p<0.001$). Interestingly, there was no significant difference between the staining

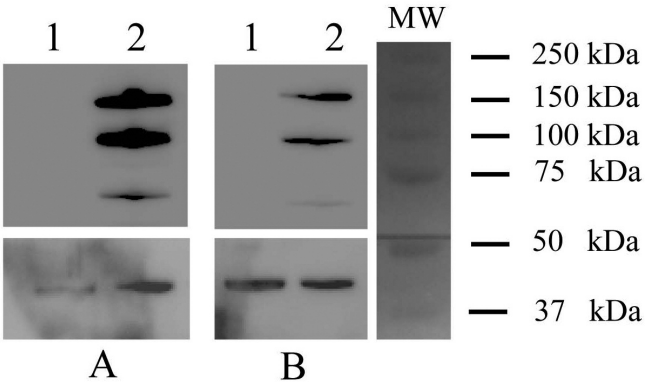

Fig. 1. Western blot validation of antibody specificity. COS7 cells transfected with a mock vector (1) or pcDNA3.1:SMARCC1:V5-His (2). **A.** anti-V5 antibody (upper) and anti-beta-actin (lower); **B.** anti-SMARCC1 (upper), anti-beta-actin (lower). MW: molecular weight marker.

patterns of high grade PIN versus non-metastatic/non-recurrent cancer specimens (Table 2), suggesting that SMARCC1 expression may be upregulated already at an early stage in some prostate cancers.

When reviewing the carcinoma specimens in more detail, we found that 19% of patients with non-metastatic/non-recurrent cancers (T1-3N0M0) had moderate to marked SMARCC1 expression (moderate (18.9%) and marked (0.5%)), whereas this was the case for 31% of the recurrent cancers (moderate (24.4%) and marked (6.1%)). Thus, SMARCC1 immunostaining was significantly stronger in recurrent cases compared to non-recurrent/non-metastatic cases ($p<0.05$). This finding was further substantiated by a logistic regression analysis, which gave an OR of 16 (CI 2-145, $p<0.05$) of recurrent cancer for patients with marked SMARCC1 staining. Moreover, 31% of patients with metastatic disease expressed moderate to marked immunostaining (moderate (20.8%) and marked (10.4%)), however, the seeming difference between metastatic disease and non-metastatic/non-recurrent disease was not statistically significant ($p=0.08$) in a correlation test. A logistic regression analysis indicated that patients with marked SMARCC1 immunostaining have an OR of 4.5 (CI 1-17, $p<0.05$) of metastases at the time of diagnosis.

Only 11% of lymph node metastases showed moderate to marked immunostaining, yet the apparent difference between SMARCC1 staining in lymph node metastases versus in metastatic primary tumours proved not to be statistically significant ($p=0.08$).

When analysing SMARCC1 immunostaining versus clinical T stage, we found a significant positive

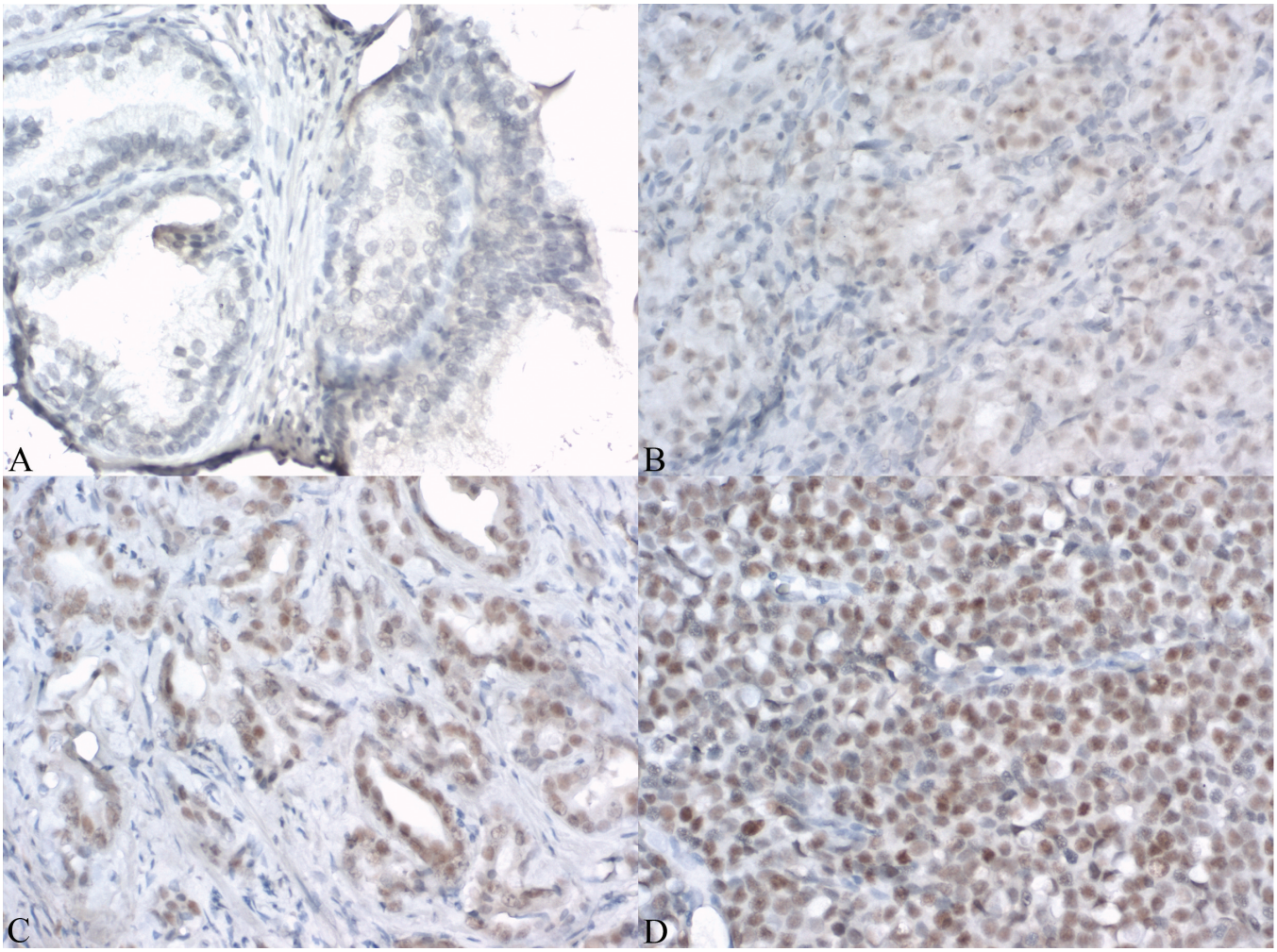

Fig. 2. Images of Smarcc1 immunostaining. **A.** Patient with benign prostate hyperplasia and no immunoreaction towards Smarcc1 protein (0). **B**. Patient with a T3aN1M0 cancer, Gleason score 8 and little Smarcc1 immunostaining (1). **C.** Patient with a T2bN0M0 cancer, Gleason score 7, displaying moderate Smarcc1 immunostaining of the nucleus (2). **D.** Patient with a T2cN0M0 cancer, Gleason score 7, displaying marked Smarcc1 immunostaining of the nucleus (3) and also discrete staining of the cytoplasm. x 500.

Table 1. Clinico-pathological distribution of the 327 prostate cancer patients.

	Non-recurrent, non-metastatic PC	Recurrent PC	Metastatic PC	Total
Clinical T stage				
T1	84 (43%)	28 (33%)	2 (4%)	114 (35%)
T2	106 (54%)	55 (66%)	20 (42%)	181 (55%)
T3	5 (3%)	1 (1%)	11 (23%)	17 (5%)
T4	0	0	15 (31%)	15 (5%)
Total	195 (100%)	84 (100%)	48 (100%)	327 (100%)
Gleason score				
5	33 (17%)	8 (10%)	0	41 (13%)
6	66 (34%)	8 (10%)	3 (6%)	77 (24%)
7	78 (40%)	54 (64%)	12 (25%)	144 (44%)
8	15 (8%)	11 (13%)	15 (32%)	41 (13%)
9	3 (2%)	3 (4%)	12 (25%)	18 (6%)
10	0	0	6 (13%)	6 (2%)
Total	195 (100%)	84 (100%	48 (100%)	327 (100%)
Serum PSA				
0 – 9.9 μg/l	70 (36%)	19 (23%)	6 (13%)	95 (29%)
10 – 19.9 μg/l	89 (46%)	32 (38%)	4 (8%)	125 (38%)
20 – 49.9 μg/l	34 (17%)	30 (36%)	15 (31%)	79 (24%)
> 50 μg/l	2 (1%)	3 (4%)	23 (48%)	28 (9%)
Total	195 (100%)	84 (100%)	48 (100%)	327 (100%)

Non-recurrent, non-metastatic PC: Prostate cancer patients who did not have metastases upon diagnosis or recurrent cancer upon follow-up. Recurrent PC: Prostate cancer patients who did not have metastases upon diagnosis but who have recurrent cancer (raising PSA) upon follow-up. Metastatic PC: Prostate cancer patients who have metastatic disease upon diagnosis.

Table 2. Clinico-pathological data versus SMARCC1 expression.

	No staining	Weak staining	Moderate staining	Marked staining	Total
Cases					
BPH	19 (68%)	9 (32%)	0	0	28 (100%)
BPC	24 (83%)	5 (17%)	0	0	29 (100%)
High grade PIN	5 (33%)	8 (53%)	2 (13%)	0	15 (100%)
Non-recurrent, Non-metastatic PC	57 (30%)	96 (51%)	36 (19%)	1 (1%)	190 (100%)
Recurrent PC	18 (22%)	39 (48%)	20 (24%)	5 (6%)	82 (100%)
Metastatic PC	14 (29%)	19 (40%)	10 (21%)	5 (10%)	48 (100%)
LN metastases	8 (47%)	7 (41%)	1 (6%)	1 (6%)	17 (100%)
Total					409
Gleason score					
5	20 (50%)	13 (33%)	7 (18%)	0	40 (100%)
6	20 (27%)	38 (51%)	16 (22%)	0	74 (100%)
7	29 (20%)	78 (55%)	30 (21%)	5 (4%)	145 (100%)
8	12 (30%)	18 (45%)	8 (20%)	2 (5%)	43 (100%)
9	8 (44%)	5 (28%)	4 (22%)	1 (6%)	25 (100%)
10	0	2 (33%)	1 (17%)	3 (50%)	11 (100%)
Total					320
Clinical T stage					
T1	35 (31%)	59 (53%)	18 (16%)	0	112 (100%)
T2	46 (26%)	86 (49%)	38 (22%)	6 (3%)	176 (100%)
T3	5 (29%)	6 (35%)	5 (33%)	1 (6%)	17 (100%)
T4	3 (20%)	3 (20%)	5 (33%)	4 (27%)	15 (100%)
Total					320

Examples of no, weak, moderate and marked staining are displayed in Figure 2a, 2b, 2c and 2d respectively. BPH: Benign prostate hyperplasia. BPC: Benign tissue from prostate cancer patients. High grade PIN: Tissue from patients presenting high grade prostate intraepithelial neoplasia. Non-recurrent, non-metastatic PC: Prostate cancer patients who did not have metastases upon diagnosis or recurrent cancer upon follow-up. Recurrent PC: Prostate cancer patients who did not have metastases upon diagnosis but who have recurrent cancer (raising PSA) upon follow-up. Metastatic PC: Prostate cancer patients who have metastatic disease upon diagnosis. LN metastases: Tissue from lymph node metastases. Clinical T stage: UICC 2002.

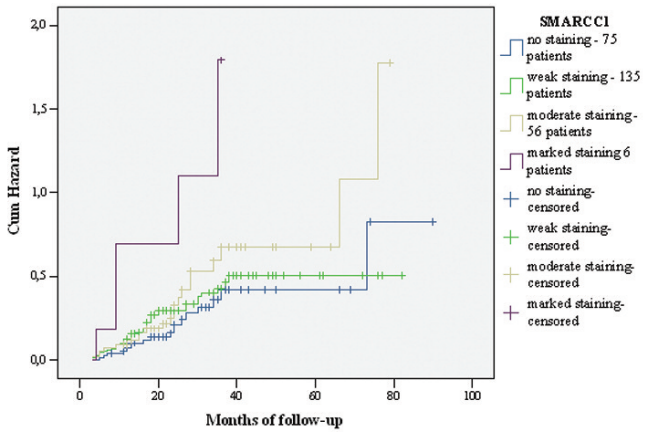

Fig. 3. Kaplan-Meyer curves on time to recurrence. According to Log Rank statistics the group showing 'marked staining' has significantly shorter time to recurrence than the 3 other groups of patients; 'no staining' ($p<0.001$), 'weak staining' ($p<0.005$) and 'moderate staining' ($p<0.05$). A Cox proportional hazard regression analysis indicates that patients with marked SMARCC1 immunostaining have an OR of 4.57 for recurrent cancer (CI 2-12, $p<0.005$).

correlation ($p<0.01$). In agreement with this, 16% of cT1 tumour patients and 35% of cT3 patients, respectively, showed high SMARCC1 expression (Table 2). We also tested whether there was a significant correlation between SMARCC1 expression and tumour differentiation. In short, 18% of Gleason score 5, 25% of Gleason score 7 and 67% of Gleason score 10 specimens showed moderate to marked immunostaining (Table 2). The correlation between SMARCC1 expression and Gleason score was statistically significant ($p<0.05$).

Neither serum PSA at the time of diagnosis or pathological T stage were associated with SMARCC1 immunostaining.

Interestingly, we found a significant correlation between SMARCC1 expression and time to disease recurrence (Fig. 3). The group of patients with marked SMARCC1 expression had a shorter time to recurrence than the three other groups of patients by log rank pairwise comparison ($p<0.05$). A Cox proportional hazard regression analysis indicates that patients with marked SMARCC1 immunostaining have an OR of 4.57 for recurrent cancer (CI 2-12, $p<0.005$).

Discussion

The major finding of this study is that SMARCC1 immunostaining is significantly increased in prostate cancer. Furthermore, our results show that SMARCC1 expression is positively correlated with Gleason score, clinical T stage, metastasis at diagnosis and time to recurrence, suggesting that it is implicated in tumour dedifferentiation, progression and recurrence.

SMARCC1 is a core subunit of the large ATP-dependent chromatin remodelling complex, hSWI/SNF, which has an important function in chromatin remodelling. The SWI/SNF complex is involved in the activation and repression of target gene transcription, associated with various aspects of cellular development, differentiation, proliferation, and tumourigenesis (Kim et al., 2001). The central ATPase subunits, BRM and BMG1, contain the catalytic remodelling activity, while the remaining subunits, e.g. SMARCC1, most likely are involved in modulation of the remodelling activity and in targeting the complex to specific promoters (Narlikar et al., 2002).

The SWI/SNF complex has been shown to modulate and transactivate the androgen receptor, and hormone dependent activation of the AR seems partly dependent on SWI/SNF action (Huang et al., 2003; Marshall et al., 2003). The mechanisms by which the SWI/SNF complex regulates AR action are largely unknown, although the subunit BAF57 has been shown to directly bind and activate the AR (Link et al., 2005).

Several studies have connected the SWI/SNF complex to carcinogenesis. It has been suggested that the SWI/SNF complex and various subunits can act as tumour-suppressors in different human cancers (Versteege et al., 1998; Sevenet et al., 1999; Wong et al., 2000; Biegel et al., 2000; Neely and Workman, 2002; Reisman et al., 2003; Roberts and Orkin, 2004). However, SWI/SNF action is governed by the diversity and plasticity of its subunit composition. Growing evidence indicates that the subunits can act either as tumour suppressive or carcinogenic factors, depending on the composition and the biological/cellular context (Klochendler-Yeivin et al., 2002; Link et al., 2005; Sun et al., 2007). Concerning PC, Link et al. (2005) showed that inhibition of other SWI/SNF subunits (BAF57 or BRM) attenuates cellular proliferation in the androgen dependent LNCaP PC cell line. Likewise, Sun et al. (2007) found that a higher expression level of the core ATPase BRG1 is associated with larger volume of prostate tumour mass.

The increased expression of SMARCC1 protein in prostate cancer reported here and in gene expression profiling studies (Lapointe et al., 2004; Varambally et al., 2005; Tomlins et al., 2007) may in part be explained by amplification of chromosome 3p21-23, as reported earlier (Tørring et al., 2007).

Recent publications have indicated that other mechanisms may also modulate the expression and activity of SMARCC1 in prostate carcinogenesis. Hong et al. (2005) found that Srg3, which is the murine homologue to SMARCC1, modulates the androgen receptor activity in the prostate in a positive feedback regulatory loop. Androgen induces expression of Srg3 through recruitment of the androgen receptor. Increasing levels of Srg3 enhance the transactivation of AR, providing a positive feedback loop that involves the coactivator SRC-1. Androgen treatment of LNCap cells, which overexpress murine Srg3, stimulates the association of AR, Srg3 and Src-1 to the PSA promoter, and thereby leads to increased transcription of the

endogenous PSA gene (Hong et al., 2005). Thus, SMARCC1 may play a role for the androgen dependent proliferation of the prostate gland during glandular development and possibly also carcinogenesis. This may elicit the positive correlation between SMARCC1 expression and tumour dedifferentiation, progression, metastasis and recurrence reported in this study.

Recently, Foster et al. (2006) demonstrated interactions between the serine/threonine kinase AKT and the hSWI/SNF chromatin remodelling complex. They showed that SMARCC1 is phosphorylated and thus activated by AKT in vitro. This is of particular interest seeing that the tumour suppressor PTEN, is inactivated in a significant proportion of prostate carcinomas, due to homozygous deletions of the chromosome 10q23.3, mutations within the gene or epigenetic modulation (reviewed by Ittmann, 1998). Inactivation of PTEN leads to constitutive activation of AKT, thereby modulating the function of the hSWI/SNF complex in general and of SMARCC1 specifically.

Besides gene expression profiling studies, few studies have investigated the expression of SMARCC1 in human cancers. DeCristofaro et al. (2001) tested SMARCC1 expression in breast cancer cell lines and found that despite high frequency of chromosomal aberration of 3p21, all tested breast cancer carcinomas were positive for SMARCC1 by Western blot analysis. Likewise, the prostate cancer cell line PC3 expresses SMARCC1, and Fukuoka et al. (2004) found expression of SMARCC1 in eight of nine lung cancer cell lines.

The finding that SMARCC1 is positively correlated to tumour dedifferentiation, progression, metastasis and time to recurrence suggests that increased expression of SMARCC1 in prostate cancer may be of importance to PC carcinogenesis and further functional studies are relevant.

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