Pathol. Oncol. Res. (2012) 18:153–160
DOI 10.1007/s12253-011-9421-8

RESEARCH

CD10 Expression in Epithelial and Stromal Cells of Non-small Cell Lung Carcinoma (NSCLC): A Clinic and Pathologic Correlation

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Received: 15 October 2010 / Accepted: 26 May 2011 / Published online: 18 June 2011

Abstract CD10 is a zinc dependent metallopeptidase, and its expression in stromal and/or epithelial cells of many carcinomas has been suggested to have prognostic value. This study investigates CD10 expression in epithelial and stromal cells of non small cell lung carcinoma (NSCLC), and evaluates its prognostic value for this tumor and its histologic subtypes. Sixty-six cases of NSCLC [35 cases of nonsquamous cell carcinoma (NSCC) and 31 cases of squamous cell carcinoma (SCC)] were analyzed immunohistochemically for CD10 antibody. Fisher's exact test and univariate survival analyses were performed. Comparison of clinicopathologic characteristics for NSCLC showed that only stromal CD10 expression had worse prognostic impact, associated with the presence of recurrence (p=0.001), death (p=0.006) and disease positivity (p=0.001). For SCC, CD10 was found to be expressed mainly in the stromal cells, and was associated with a decreased survival (p=0.000) and disease free survival (p=0.000). CD10 expression was restricted to the epithelial cells in NSCC and associated with an increased disease free survival (p=0.036). Stromal CD10 expression apppears to be a worse prognostic factor in NSCLCs. CD10 which is expressed in different cell components of SCC and NSCC appears to have opposing effects on the behaviour of these histologic types.

Keywords CD10 · Carcinoma · Lung · Stromal cells · Epithelial cells

Abbreviations

NSCLC	Nonsmall cell lung carcinoma
NSCC	Nonsquamous cell carcinoma
SCC	Squamous cell carcinoma

Introduction

CD10/ neutral endopeptidase 24.11 (NEP) is a cell surface zinc dependent 90–110 kDa metallopeptidase [1, 2] which is widely expressed in various normal tissues and in epithelial, stromal or both components of various malignancies [2–9]. It plays an important role in the maintenance of homeostasis in normal tissues by hydrolyzing multiple naturally occurring bioactive peptides and down regulating the induced responses to peptide hormones [10]. It appears that its role in tumor progression differs according to cell compartment in which it is expressed and tumor type. Although contradictory reports have been published, loss or decrease of CD10 expression in tumor cells has been shown to contribute to the development or the progression in many types of malignancies, including renal cancers, invasive bladder cancer, poorly differentiated stomach cancer, small cell and non-small cell lung cancer, and prostate cancer [11–16].

Contrary to the suggested impact of tumor cell CD10 expression on tumor behavior, many reports have shown a

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significant correlation of stromal cell CD10 expression with tumor progression in various cancers, such as melanoma, colorectal carcinoma, well differentiated gastric cancer, squamous cell carcinomas of nasopharynx, skin and oral cavity, cutaneous basal cell carcinoma, and breast cancers [17–24].These studies suggest that CD10 plays an important role in tumor progression by degrading the extracellular matrix and promoting the remodalization of the stroma.

To our knowledge, there are only a few numbers of studies on the expression of CD10 in NSCLC which investigated only tumor cell CD10 expression and its prognostic significance [25, 26]. On the other hand, CD10 expression in stromal cells of NSCLCs and prognostic significance of stromal cell CD10 expression has not been reported so far.

In this study we investigated immunohistochemically CD10 expression in tumor cells and stromal cells of NSCLC, and correlated this with several clinicopathologic parameters, such as squamous and nonsquamous histologic types, clinical stage, metastases, local recurrences, lymph node status, and death related to disease, and disease positivity. In addition, prognostic parameters are compared between stromal or tumor cell CD10+ and CD10- groups in SCC and NSCC, separately.

Materials and Methods

Archival material from 66 NSCLCs was studied, including 31 SCC and 35 NSCC (21 adenocarcinoma, six large cell carcinoma, three large cell neuroendocrine carcinoma, three sarcomatoid carcinoma and two adenosquamous carcinoma). Patients' clinical data were obtained from hospital charts. The following histopathologic and clinical data were recorded: age, sex, histologic type, death, recurrence, metastases, stage, lymph node status and disease positivity (cases that have recurrence, metastases or death were grouped together as disease positive). Tumors were histologically classified into two groups: SCC [27] and NSCC [28]. All patients were staged according to TNM system: 10 (15%) cases were at stage IA, 20 (30%) cases were at stage IB, 3 (4%) cases were at stage IIA, 13 (20%) cases were at stage IIB, 9 (%14) cases were at stage IIIA, 7 (11%) cases were stage IIIB and 4 (6%) cases were at stage IV [29]. When divided into two groups, 46 (69.7%) patients were at early stages (Stages IA, IB, IIA and IIB), and 20 (30.3%) patients were at late stages (Stages IIIA, IIIB, and IV). The clinicopathologic characteristics of the 66 patients are summarized in Table 1.

Immunohistochemistry Sections from paraffin-embedded tissue blocks were taken on lysine-coated slides. After deparafinization and rehydration, slides were placed in a

Table 1 Patient's characteristics

Parameters	No. (%)
Sex	
Male	59 (89%)
Female	7 (11%)
Stage	
StageIA	10 (15%)
Stage IB	20 (30%)
StageIIA	3 (4%)
StageIIB	13 (20%)
StageIIIA	9 (14%)
Stage IIIB	7 (11%)
StageIV	4 (6%)
Stage	
Early	46 (69.7%)
Advanced	20 (30.3%)
Lymph node metastases	
Positive	21 (31.8%)
Negative	45 (68.2%)
Metastases	
Positive	23 (34.8%)
Negative	43 (65.2%)
Metastases time; range, mean ± SD	2 to 43 months; 18.22±12.47
Recurences	
Positive	12 (18.2%)
Negative	54 (81.8%)
Recurrens time, mean ± SD	2 to 56 months; 16.58 ±17.38
Ex	
Positive	20 (30.3%)
Negative	44 (66.7%)
Ex time; range, mean ± SD	1 to 84 months; 31.8 ±25.53
Disease positivity	
Positive	34 (48.5%)
Negative	32 (51.5%)
Disease time; range, mean ± SD	1 to 84 months; 17. 74±16.43
Histologic type:	
SCC	31 (47%)
NSCC	35 (53%)
Age in years	
Range	43–85
Mean ± SD	62.80±10.96
Size in cm	
Range	0.8 to11 cm
Mean ± SD	4.63±2,63 cm
Follow up period	
Range	1–86 months
Mean ± SD	46.76±21.24 months

microwave-compatible plastic jar filled with 10 mm EDTA (pH 8.0), heated for 30 min, than washed with phosphate buffered saline (PBS, pH 7.2). Endogenous peroxidase activity was quenched with hydrogen peroxide. The tissue sections were than incubated with monoclonal antibody to CD10 (NCL-CD10-270, Novocastra laboratories, Newcastle,UK) in a 1/50 dilution for 1 h at room temperature. Binding of CD10 was detected using the strepavidin-biotin immunoperoxidase method. Diaminobenzidine was used as a chromogen.

The immunostaining results of CD10 in stromal and neoplastic cells were evaluated separately. For this evaluation, both cytoplasmic and membranous labeling were taken into account. The immune expression was regarded as positive when more than 10% of either the stromal or neoplastic cells were positive [18, 24]. For statistical analysis, cases were categorized into three groups according to CD10 expression patterns: epithelial, stromal, and both epithelial and stromal (overall).

Statistical Analysis The data were collected, tabulated and statistically analyzed, using a personnel computer with 'Statistical Package for the Social Sciences (SPSS), version 15′. Comparison between CD10+ and CD10—groups regarding clinicopathologic parameters was assessed by Fishers exact test. Survival time was calculated starting from the date of surgery. The end of the follow-up period was May 2010. Survival analyses for censored data were performed using the Kaplan-Meier method. The log- rank test was used to compare survival data. The critical level of statistical significance was $p<0, 05$.

Results

This study included 59 males and seven females with ages ranging from 43 to 85 years (mean 62.8±10.96 years).

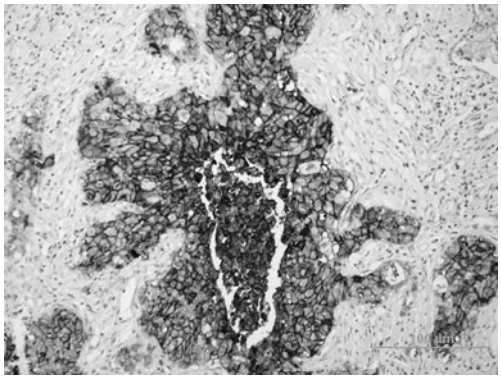

Fig. 2 Squamous cell carcinoma with strong CD10 expression in tumour cells (immunohistochemistry for CD10 antibody, original magnification X 20)

There were 31 cases of SCC and 35 cases of NSCC. Survival data were available for 64 patients. At the time of analysis, the follow-up period of 66 patients ranged from 1 to 86 months (46.76±21.24). 23 cases had metastasis and 12 cases had recurrence during the follow up. Mean times for metastasis and recurrence were 18.22±12.47 months and 16.58±17.38 months, respectively. Twenty patients died of their disease during the follow up (Table 1).

Evaluation of immunohistochemical stain for CD10 in peritumoral normal lung parenchyma showed no CD10 positivity in pneumocytes or bronchial epithelium. Only endothelial cells of alveolar capillaries were strongly positive, whereas endothelial cells of larger vessels were negative. Of 66 NSCLC cases, 25 cases (38%) showed CD10 expression. Positivity in tumor cells, in stromal cells and in both cell compartments of all cases was 18% (12/66), 15% (10/66) and 5%(3/66), respectively. While cytoplasmic or membranous staining was seen in tumor cells, only cytoplasmic staining was observed in stromal cells (Figs. 1, 2, 3).

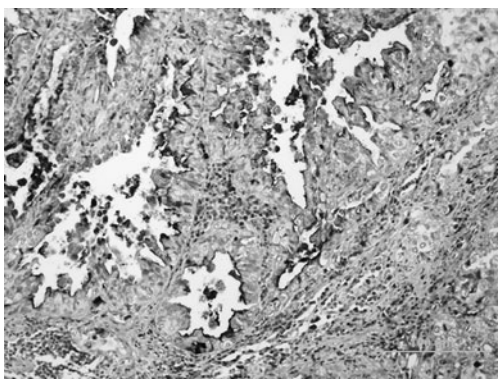

Fig. 1 CD10 expression in epithelial cells of adenocarcinoma with luminal membranouse staining pattern (immunohistochemistry for CD10 antibody, original magnification X 20)

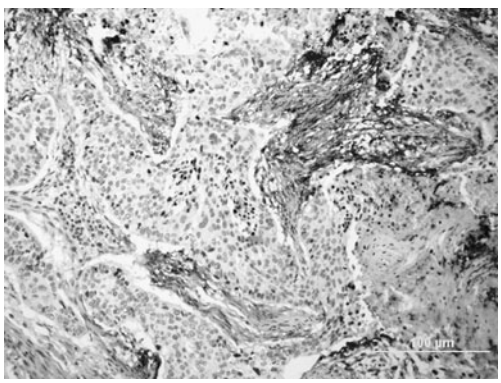

Fig. 3 Squamous cell carcinoma with strong CD10 expression in stromal cells (immunohistochemistry for CD10 antibody, original magnification X 20)

Comparison of clinicopathologic characteristics between CD10 positive and negative groups in all cases without consideration of its expression in any of the cell compartments revealed no statistically significant differences for clinical stage, metastases, recurrence, death, lymph node status, disease positivity, or histologic type (Table 2).

For the evaluation of the relation of stromal and tumor cell CD10 expression to prognostic parameters, three cases which had both stromal and tumor cell CD10 positivity were included in both stromal cell CD10 positive(10+3:13) and tumor cell CD10 positive (12+3:15 cases) groups. As a result, no significant differences were detected when these clinicopathologic parameters were compared between tumor cell CD10 positive (15 cases) and negative groups (51 cases). The tendency for the tumor cell CD10 positive group to show decreased metastases failed to reach statistical significance (p=0.065). Although, it was not statistically significant (p=0.086), the incidence of CD10 positivity in tumor cells was higher in NSCCs than SCCs. Among the tumor cell CD10 positive 15 cases, 4 (27%) were SCC and 11 (73%) were NSCC.

On the other hand, there were significant differences between stromal cell CD10 positive (13 cases) and negative (53 cases) groups regarding histologic type (p=0.000), recurrence (p=0.001), death (p=0.006) and disease positivity (p=0.001). Those cases with stromal CD10 positivity showed statistically significant association with increased recurrence, death, disease positivity and squamous cell histologic type. All the stromal CD10 positive cases (13 cases) were SCCs. In addition, Kaplan Meier disease free survival curve showed significant difference between stromal cell CD10 positive and negative groups (p=0.000) (Fig. 4).

Since there was an obvious difference in CD10 + cell compartment between SCCs and NSCCs, the relation of CD10 positivity to prognostic parameters was investigated for SCCs and NSCCs, separetely. Considering SCCs, statistically significant correlation was found between overall (stromal and epithelial) CD10 positivity and clinical parameters such as recurrence (p=0.011) , metastases (p=0.031), death (p=0.002) and disease positivity (p=0.000). While stromal cell CD10 positivity was associated with an increased recurrence (p=0.004), death (p=0.009) and disease positivity (p=0.001), tumor cell CD10+cases had no such relations with prognostic parameters.

For NSCCs, expression of CD10 was found only in tumor cells and it showed a statistically significant inverse correlation with disease positivity (p=0.027) and a near significant inverse relation with metastases (p=0.055). In other words, incidences of metastases and disease positivity were higher in CD10 negative tumors. Comparison of prognostic parameters for SCCs and NSCCs according to CD10+ and—cases are shown in Tables 3 and 4, respectively.

According to the results of univariate analyses estimated by the longrank test, for SCCs expression of CD10 (overall, stromal or epithelial, respectively) was significantly associated with decreased disease free survival (P=0.000, p=0.000, P=0.008). On the otherhand, for NSCCs, univariate analysis showed that CD10 negativity and clinical stage were associated with poor outcome (p=0.036, p=0.022, respectively). Kaplan Meier disease free survival curve for SCCs and NSCCs according to CD10+ and CD10- cases are shown in Figs. 5 and 6, repectively.

Table 2 Comparison of clinicopathologic characteristics between CD10 positive and CD10 negative groups in all cases

Parameters		CD10 overall		Test of sig. P	CD10 tumor cell		Test of sig. P	CD10 stromal cell		Test of sig. P
		Positive no. (%)	Negative no. (%)		Positive no. (%)	Negative no. (%)		Positive no. (%)	Negative no. (%)	
Type	Squamous (n:31)	14 (45%)	17 (55%)	P=0.313	4 (13%)	27 (87%)	P=0.086	13 (42%)	18 (58%)	P=0.000
	Nonsquamous (n:35)	11 (31%)	24 (69%)		11 (31%)	24 (69%)		0 (0%)	35 (100%)	
Stage	Early (n:46)	18 (39%)	28 (61%)	P=0.790	11 (24%)	35 (76%)	P=1	9 (20%)	37 (80%)	P=1
	Late (n:20)	7 (35%)	13 (65%)		4 (20%)	16 (80%)		4 (20%)	16 (80%)	
Lymph node	Positive (n:21)	9 (43%)	12 (57%)	P=0.596	7 (33%)	14 (67%)	P=0.210	4 (19%)	17 (81%)	P=1
	Negative (n: 45)	16 (36%)	29 (64%)		8 (18%)	37 (82%)		9 (20%)	36 (80%)	
Recurrence	Positive (n:12)	7 (58%)	5 (42%)	P=0.186	1 (8%)	11 (92%)	P=0.270	7 (58%)	5 (42%)	P=0.001
	Negative (n:54)	18 (33%)	36 (67%)		14 (26%)	40 (74%)		6 (11%)	48 (89%)	
Metastase	Positive (n:23)	9 (39%)	14 (61%)	P=1	2 (9%)	21 (91%)	P=0.065	7 (30%)	16 (70%)	P=0.192
	Negative (n: 43)	16 (37%)	27 (63%)		13 (30%)	30 (70%)		6 (14%)	37 (86%)	
Exitus	Positive (n:20)	10 (50%)	10 (50%)	P=0.161	4 (20%)	16 (80%)	P=1	8 (40%)	12 (60%)	P=0.006
	Negative (n: 44)	13 (30%)	31 (70%)		10 (23%)	34 (77%)		4 (9%)	40 (91%)	
Disease	Positive (n: 34)	15 (44%)	19 (56%)	P=0.319	6 (18%)	28 (82%)	P=0.384	12 (35%)	22 (65%)	P=0.001
	Negative (n:32)	10 (31%)	22 (69%)		9 (28%)	23 (72%)		1 (3%)	31 (97%)	

Sig, significance; Fisher's exact test

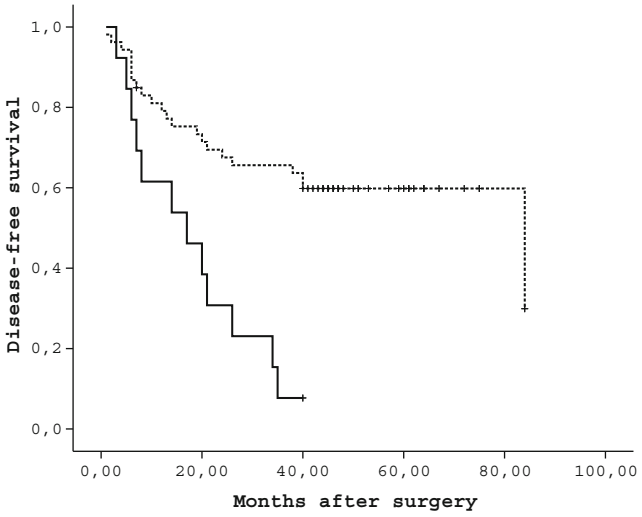

Fig. 4 Disease free survival curves according to Kaplan Meier for 66 patients of the study group according to stromal CD10 expression (*solid lines*) or absence of expression (*dottled line*), $p=0.000$, logrank method

Discussion

In this study, we found that normal lung parenchyma has an expression of CD10 in alveolar capillaries exclusively, with no expression in pneumocytes or bronchial epithelium, which is in accordance with the results of Kristiansen et al., while contradicts some other previous reports [14, 30].

Although, in many carcinomas CD10 expression had been investigated in stromal cells or in both tumor cell and stromal cell compartments, the limited number of studies in NSCLCs reported its expression only in tumor cells, which ranged from 12.5% to 31.1%. In concordance with the published expression rates, present study showed tumor cell CD10 expression in 23% of NSCLC [7, 14, 25, 26]. Incidence of stromal expression of CD10 in NSCLC which has not been reported so far, was 20% and overall (both stromal and tumor cell) expression rate was 38%.

There are also only a few studies on the prognostic value of CD10 expression in NSCLCs, which investigated the relation of CD10 expression in tumor cells with prognostic parameters. In one of these studies, Tokuhara et al. reported that CD10 positive tumors had significantly higher 5-year survival than those whose tumors were CD10 negative [26]. In another study by Kristiansen et al., no associations of CD10 expression in tumor cells of NSCLC with patient survival or any other clinicopathological parameters were found [25].

In this study, we found that while overall (tumor cell+stromal cell) CD10 positivity in NSCLC cases was not associated with any of the tested clinicopathologic parameters, stromal CD10 positivity was restricted to squamous cell histologic type and associated with increased recurrences, death and disease positivity. In accordance with our result in NSCLCs, increased stromal cell expression of CD10 had been related to tumour progression and metastases in different tumors, such as malignant melanoma, colorectal tumors, differentiated gastric carcinomas, breast cancers, oral cavity SCCs, nasopharyngeal SCCs, and cutaneous carcinomas, especially for basal cell carcinomas [17–24, 31]. It was postulated that due to structural similarities of CD10 to matrix metalloproteinase's (MMPs), CD10 could create a microenvironment that facilitates cancer cell invasion and metastases [32, 33].

Table 3 Comparison of clinicopathologic characteristics between CD10 positive and CD10 negative groups in SCC

Parameters		CD10 overall		Test of sig. *P*	CD10 tumor		Test of sig. *P*	CD10 stromal		Test of sig. *P*
		Positive no. (%)	Negative no. (%)		Positive no. (%)	Negative no. (%)		Positive no. (%)	Negative no. (%)	
Stage	Early (n:20)	9 (45%)	11 (55%)	$P=1$	2 (10%)	18 (90%)	$P=0.601$	9 (45%)	11 (55%)	$P=0.718$
	Late (n:11)	5 (45%)	6 (55%)		2 (18%)	9 (82%)		4 (36%)	7 (64%)	
Lymph node	Positive (n: 9)	5 (56%)	4 (44%)	$P=0.693$	3 (33%)	6 (67%)	$P=0.063$	4 (44%)	5 (56%)	$P=1$
	Negative (n: 22)	9 (41%)	13 (59%)		1 (5%)	21 (95%)		9 (41%)	13 (59%)	
Recurrence	Positive (n: 8)	7 (88%)	1 (12%)	$P=0.011$	1 (12.5%)	7 (87.5%)	$P=1$	7 (88%)	1 (12%)	$P=0.004$
	Negative (n:23)	7 (30%)	16 (70%)		3 (13%)	20 (87%)		6 (26%)	17 (74%)	
Metastase	Positive (n:11)	8 (73%)	3 (27%)	$P=0.031$	1 (9%)	10 (91%)	$P=1$	7 (64%)	4 (36%)	$P=0.128$
	Negative(n: 20)	6 (30%)	14 (70%)		3 (15%)	17 (85%)		6 (30%)	14 (70%)	
Exitus	Positive (n:11)	9 (82%)	2 (18%)	$P=0.002$	3 (27%)	8 (73%)	$P=0.126$	8 (73%)	3 (27%)	$P=0.009$
	Negative (n: 19)	4 (21%)	15 (79%)		1 (5%)	18 (95%)		4 (21%)	15 (79%)	
Disease	Positive (n: 17)	13 (76%)	4 (24%)	$P=0.000$	4 (24%)	13 (76%)	$P=0.107$	12 (71%)	5 (29%)	$P=0.001$
	Negative (n: 14)	1 (7%)	13 (93%)		0 (0%)	14 (100%)		1 (7%)	13 (79%)	

Sig, significance; Fisher's exact test

Table 4 Comparison of clinicopathologic characteristics between CD10 positive and CD10 negative groups in NSCC

Parameters		CD10 tumor		Test of sig. *P*
		Positive no. (%)	Negative no. (%)	
Stage	Early (n:26)	9 (35%)	17 (65%)	*P*=0.685
	Late (n:9)	2 (22%)	7 (78%)	
Lymph node	Positive (n: 12)	4 (33%)	8 (67%)	*P*=1
	Negative (n: 23)	7 (30%)	16 (70%)	
Recurrence	Positive (n: 4)	0 (0%)	4 (100%)	*P*=1
	Negative (n:31)	11 (35%)	20 (65%)	
Metastase	Positive (n:12)	1 (8%)	11 (92%)	*P*=0.055
	Negative(n: 23)	10 (43%)	13 (57%)	
Exitus	Positive (n:9)	1 (11%)	8 (89%)	*P*=0.255
	Negative (n: 25)	9 (36%)	16 (64%)	
Disease	Positive (n: 17)	2 (12%)	15 (88%)	*P*=0.027
	Negative (n: 18)	9 (50%)	9 (50%)	

Sig, significance; Fisher's exact test

The reported emergence of stromal CD10 expression as a worse prognostic factor especially in SCCs of extra pulmonary sites, and our finding of higher stromal CD10 expression in pulmonary SCCs, prompted us to test the relation of CD10 positivity with prognostic parameters in SCCs and NSCCs, separately [20–23]. Similar to the results of other studies in SCCs of non-pulmonary sites, statistically significant correlation was found between stromal CD10 positivity and recurrence (p=0.004), death (p=0.009) and disease positivity (p=0.001) in pulmonary SCCs.

On the other hand in 34 NSCCs, CD10 expression was restricted to tumor cells and it showed a statistically significant inverse correlation with disease positivity (p=0.027) and a near significant inverse relation with metastases (p=0.055). CD10/NEP hydrolyses small bioactive peptides, which are growth factors for normal airway epithelial cells and lung cancer. Low CD10 expression could increase local concentrations of neuropeptides and promote lung tumor growth [14, 15]. Cohen at al. found an expression rate immunohistochemistry of 12.5%(n: 24) in NSCLCs and interpreted this in comparison to lung parenchyma as a down regulation [14]. The hypothesis of CD10 acting as a down regulated tumor suppressor gene was supported by in vitro demonstration of a link between the inhibition of CD10 expression and increased proliferation rates [28]. This endorses the hypothesis, that loss of CD10 expression could be linked to a more aggressive tumor behavior. Thus, in accordance with the results of Takuhara et al, our finding of an inverse relation of tumor cell CD10 expression with metastases and disease positivity in NSCCs supports the suggestion that it might be a good prognostic indicator in pulmonary NSCCs [26].

However, contradicting results regarding the impact of both stromal and epithelial CD10 expression on prognostic

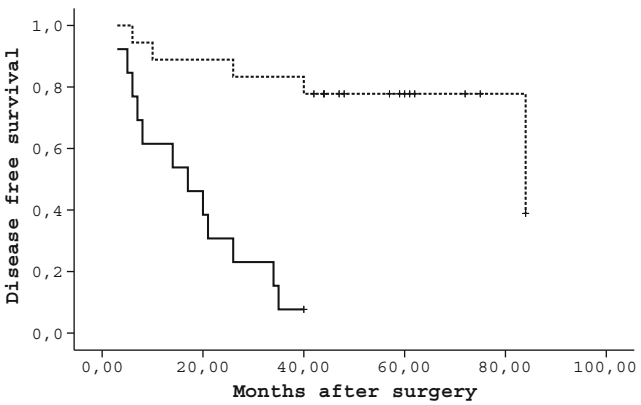

Fig. 5 Disease free survival curves according to Kaplan Meier for 31 SCC cases of the study group according to stromal CD10 expression (*solid lines*) or absence of expression (*dottled line*), p=0.000, logrank method

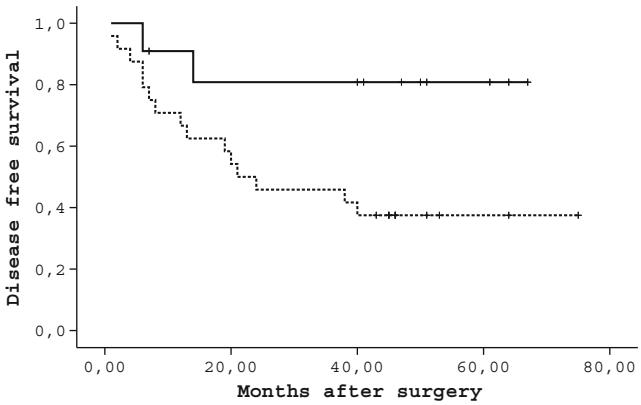

Fig. 6 Disease free survival curves according to Kaplan Meier for 35 NSCC cases of the study group according to CD10 expression (*solid lines*) or absence of expression (*dottled line*), p=0.036, logrank method

variables have been reported in several carcinomas of different sites. For example, in pancreatic endocrine tumors and bladder carcinoma, no significant correlation was found between stromal CD10 expression and any of the tested histopathologic indicators of poor outcome, while tumor cell expression was found to be related with worse prognostic factors [34, 35]. In ovarian carcinomas, CD10/NEP expression in stromal cells and tumour cells was found to act similarly and a possible role for this enzyme as a suppressor of ovarian carcinoma was proposed [27]. Contrary to its suggested function like MMPs, transfection of ovarian carcinoma cell lines with NEP resulted in decrease in MMP-2 activity which was in part reversed by the addition of NEP inhibitors.

The explanation for these findings is not clear and the exact role of CD10 in carcinogenesis is currently unknown. First of all, CD10 appears to have opposing enzymatic functions. Secondly, other mechanisms independent of the enzyme activity might be involved. In fact, Sumitomo et al., suggested an inhibitory role of CD10 in prostate cancer cell migration via a non-enzymatic protein-protein interaction [36]. It appears that CD10 might have different roles and its contribution to carcinogenesis seems to differ in various carcinomas. In fact, our finding of opposing prognostic value of CD10 expression for Pulmonary NSCC and SCC cases supports this hypothesis. Several studies showed that CD10 levels, in vitro, are influenced by several factors. Certain cytokines such as interleukin-1α, tumor necrosis factor, and interleukin-6 and granulocyte macrophage colony stimulating factor increase lung fibroblasts CD10 expression during the inflammatory process [37, 38]. On the other hand, transforming growth factor-β1 could decrease CD10 activity by reducing gene transcription or mRNA stability [39]. Furthermore, CD10 activity may be regulated by prostaglandin synthesis and cAMP [38]. These factors secreted from the tumor cells may stimulate or inhibit stromal cell expression/ activity of CD10, singularly or in combination. It can be speculated that the differences in the combination of these factors secreted by different tumor types might contribute variable expression and activity of CD10 in different tumors.

In conclusion, we demonstrated that while CD10 expression was a worse prognostic factor with decreased overall and disease free survival for SCCs regardless of the stromal or epithelial expression, it's expression in tumor cells was a better prognostic factor with increased overall and disease free survival for NSCC. Thus, it can be speculated that expression of CD10 in different cell compartments and it's opposing effect on tumor behaviour might be related to squamous or nonsquamous differentiation in NSCLCs. It's significance as a prognostic factor in NSCLCs remains to be investigated in larger series.

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