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Expression and significance of E-cadherin, N-cadherin, transforming growth factor-β1 and Twist in prostate cancer

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ABSTRACT

Objective: To study the expression of E-cadherin, N-cadherin, TGF-β1 and Twist protein and investigate its significance in the occurrence and development of prostate cancer. **Methods:** The expression of E-cadherin, N-cadherin, TGF-β1 and Twist protein in 59 prostate cancer tissues and 21 adjacent tissues were detected by immunohistochemical SABC staining, and the correlation with clinicopathological features was analyzed. **Results:** Positive rates of E-cadherin, N-cadherin, TGF-β1 and Twist were 32.2%, 54.2%, 71.2% and 74.6%, respectively, in prostate cancer tissues and 85.7%, 9.52%, 19.0% and 9.52%, respectively, in cancer-adjacent tissues, with significant differences between the two groups ($P<0.05$). The reduced expression of E-cadherin was related to the differentiation of prostate cancer tissues and PSA level, but was not associated with clinical stage, lymph node metastasis, bony metastasis and age. The increased expression of N-cadherin, TGF-β1 and Twist was related to the differentiation of prostate cancer tissues, clinical stage, lymph node metastasis, bony metastasis, but not to age. The difference in positive expression of N-cadherin and TGF-β1 was significant between PSA≤20 μg/L group and PSA>20 μg/L group, but the positive expression of Twist was not significant between groups. The expression of E-cadherin was highly negatively correlated with that of N-cadherin and also highly negatively correlated with that of Twist. The expression of TGF-β1 was correlated with those of E-cadherin, N-cadherin and Twist. **Conclusions:** The reduced expression of E-cadherin, abnormal expression of N-cadherin, transformation form E-cadherin to N-cadherin and the increased expression of TGF-β1 and Twist play an important role in the occurrence and development of prostate cancer.

1. Introduction

Epithelial-mesenchymal transition (EMT) was first proposed by Greenberg and Hay in 1982, who found that the lens epithelial cells cultured in the gel can morphologically transform into the mesenchyme-like cells with pseudopodia[1]. EMT persists throughout the mammalian embryonic development and also exists in the pathophysiological processes including tissue healing, organ fibrosis and tumor cell infiltration and metastasis. EMT is mainly characterized by loss of epithelial cell polarity, gain of mesenchymal cell properties, and abnormal expression of E-cadherin and N-cadherin. Transforming growth factor-β1 (TGF-β1) is considered the master molecule in the genesis of EMT in mammals[2]. Twist is a basic helix-loop-helix transcription factor and plays a critical role in the regulation of EMT[3]. Prostate cancer is a common malignant tumor in the urinary system and its mortality rate ranks second, only after lung cancer, among all malignant tumors in Europe and America[4,5]. Recently, with acceleration of aging process, changes in life style and diets and improvement in diagnostic technique, the incidence of prostate cancer in gradually increasing in China. In prostate cancer patients, cancer cells easily separate from primary foci because of poor cell-cell adhesion and invade adjacent tissue and organs, leading to metastasis of lymph nodes, bone or distal organs and finally resulting in a high

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malignant potential with poor biological behaviors and prognosis. To validate whether prostate cancer acquires its highly invasive malignant biological behaviors via EMT, we detected the expression levels of EMT related proteins including E-cadherin, N-cadherin, TGF-β1 and Twist1 in prostate cancer tissue and adjacent tissue and investigated the role and significance of EMT in the incidence and development of prostate cancer.

2. Materials and methods

2.1. Experimental specimens

Tissue specimens were harvested from 59 patients who underwent radical prostatectomy or prostate puncture in our Hospital from 2008 to 2011 and pathologically diagnosed as primary prostate cancer. Simultaneously, tissues around the prostate cancer foci were harvested from 21 prostate cancer patients as controls. The patients who received anti-tumor treatments prior to surgery were not included in this study. The included average age of prostate cancer patients were 68 (range, 55-84) years old. According to the Gleason grading system, prostate cancer can be classified, with a score of 2-4 being well differentiated, 5-7 moderately differentiated and 8-10 poorly differentiated. The selected prostate cancer specimens consisted of well differentiated (n=18), moderately differentiated (n=22) and poorly differentiated cancer tissues (n=19). Serum prostate-specific antigen (PSA) was < 10 μg/L (n=8), 10-20 μg/L (n = 13) and > 20 μg/L (n=38). The Whitmore-Jewett staging system was used for grading experimental specimens. Stage A, cancer cells were found only in pathological examination; stage B, positive clinical symptom and cancerous tubercle only in the prostate gland; stage C, tumor cells have spread outside the covering of the prostate gland to tissues around the prostate gland but not to the lymph nodes; stage D, cancer cells have metastasized.

According to the known data (preoperative: B ultrasound images, pelvic CT and MRI images, bone scanning images of the whole body, chest X-ray image; intraoperative records: tumor size and morphology, tumor cell invasion or not, pelvic lymph node swelling or not; postoperative: pathological results), 59 patients with prostate cancer were categorized according to their clinical stages: 26 patients in stages A, B, 14 patients in stage C, and 19 patients in stage D. Among these included patients with prostate cancer, 27 underwent radical prostatectomy, 15 medical castration combined with antiandrogen treatment, 9 bilateral orchidectomy combined with antiandrogen treatment, 5 transurethral resection of the prostate gland and 3 underwent only prostatic puncture without any other treatments.

2.2. Main reagents

Rabbit anti-human E-cadherin polyclonal antibody (dilution 1:50) was purchased from Bioss Biotechnology Co.,Ltd., Beijing, China; rabbit anti-human N-cadherin (dilution 1:50), TGF-β1 (dilution 1:100) and Twist polyclonal antibodies (dilution 1:100) were purchased from Santa Cruz Biotechnology, Santa Cruz, CA, USA. Immunohistochemical SABC reagent kit, DAB and secondary antibodies were purchased from Boster, Wuhan, China.

2.3. Methods

According to kit instructions, experiments were performed using immunohistochemical SABC method. Precisely, paraffin specimens were sliced into 4 μm sections, toasted at 60 ℃ in the thermostat oven, de-waxed by xylene, and dehydrated through ethanol series (60%-100%). After PBS (pH=7.4) washes, the sections were treated with 3% H_2O_2 to inactivate endogenous peroxydase and with 0.01 M sodium citrate solution (pH=6.0) for microwave antigen retrieval. Subsequently, the sections were blocked with 10% normal goat serum and treated with primary antibody at 4 ℃ overnight. After PBS (pH=7.4) washes, the sections were incubated at 37 ℃ after addition of secondary antibodies, treated with SABC solution, developed with DAB, slightly counterstained with hematoxylin, routinely dehydrated, mounted and finally observed under the microscope. Positive control images were provided by Boster, Wuhan, China. PBS, rather than primary antibody, was used as a negative control.

2.4. Result evaluation

E-cadherin-positive cells exhibited yellow or dark brown particles in the cellular membrane. Under 400-fold optical microscope, E-cadherin-positive cells in five different fields of view were counted. The results were evaluated according to the percentage of E-cadherin-positive cells in total cells: ≥ 90% indicates E-cadherin-positive expression and <90% E-cadherin-negative expression.

N-cadherin-positive cells exhibited yellow or dark brown particles in the cytoplasm (or) cellular membrane. According to the method described by Lascombe *et al*[6], results were evaluated using semi-quantitative method: the percentage of positive cells ≥5% indicates N-cadherin-positive expression and <5% N-cadherin-negative expression.

TGF-β1-, Twist-positive cells exhibited dark brown particles in the cytoplasm and (or) a small number of nuclei. Semi-quantitative integration was used for grading TGF-β1-, Twist expression based on positive cell percentage and staining intensity. The positive cell percentage was scored 0-3 from < 5%, 5%-25%, 26%-75%, to > 75% in order. The staining intensity was scored 0-2 from none, faint to strong staining in order. The grading criteria for TGF-β1 and Twist expression was determined by the scores given as the sum of positive cell percentage and staining intensity scores: ≤ 1.9 points being "-", 2-2.9 being "+", 3-3.9 points being

"++", ⩾ 4 points being "+++". "-, +" was designated as low expression (negative), and "++, +++" as high expression (positive).

2.5. Statistical analysis

All data were statistically processed using SPSS13.0 software. Comparisons of E-cadherin, N-cadherin, TGF-β1 and Twist expression among groups were performed using x^2 test or x^2 trend test and Yates was used when necessary. Correlations among E-cadherin, N-cadherin, TGF-β1 and Twist expression was analyzed with Spearman's rank correlation. A level of $P<0.05$ was considered statistically significant.

3. Results

3.1. E-cadherin expression

E-cadherin was normally expressed in the cellular membrane. E-cadherin expression was significantly lower in the prostate cancer tissue than in the adjacent tissue [32.2% (19/59) *vs*. 85.27% (18/21), $P<0.05$; Table 1]. The expression rate of N-cadherin-positive cells in the well differentiated, moderately differentiated and poorly differentiated groups was 50.0%, 31.8% and 15.8%, respectively, showing a decreasing tendency (x^2trend=4.87, $P<0.05$). E-cadherin expression was significantly lower in the serum PSA >20 μg/L group than in the serum PSA⩽20 μg/L group ($P<0.05$). E-cadherin expression was not correlated with the clinical pathological factors including clinical stage, age, lymph node metastasis or bone metastasis ($P>0.05$; Table 2).

3.2. N-cadherin, TGF-β1 and Twist expression

N-cadherin was mainly expressed in the cytoplasm and cellular membrane (Figure 1). N-cadherin expression was significantly higher in the prostate cancer tissue than in the adjacent tissue (54.2% *vs*. 9.52%, $P<0.05$). TGF-β1 was mainly expressed in the cytoplasm and scattered in the nucleus (Figure 2). TGF-β1 expression was significantly higher in the prostate cancer tissue than in the adjacent tissue (71.2% *vs*. 19%, $P<0.05$). Twist was mainly expressed in the cytoplasm and scattered in the nucleus (Figure 3). Twist expression was significantly higher in the prostate cancer tissue than in the adjacent tissue (74.6% *vs*. 9.52%, $P<0.05$; Table 1). With decrease in degree of differentiation of prostate cancer cells, N-cadherin, TGF-β1, Twist expression tended to be increased (x^2trend = 4.47, $P<0.05$; x^2 trend = 6.88, $P<0.05$; x^2 trend = 7.38, $P<0.05$). N-cadherin, TGF-β1 and Twist expression rates were significantly lower in the stages A, B than in the stages C, D ($P<0.05$), significantly higher in patients with lymph node metastasis than in patients without ($P<0.05$), and significantly higher in patients with bone metastasis than in patients without ($P < 0.05$). N-cadherin, TGF-β1 and Twist expression did not correlate with patient's age ($P>0.05$). N-cadherin and TGF-β1 expression rates were significantly higher in the serum PSA > 20 μg/L group than in the serum PSA ⩽ 20

Table 1
Comparisons of E-cadherin, N-cadherin, TGF-β1 and Twist expression in the prostate cancer tissue and adjacent tissue.

Protein	Prostate cancer tissue (n=59)		Adjacent tissue (n=21)		x^2	P
	Positive	Negative	Positive	Negative		
E-cadherin	19	40	18	3	17.84	0.000
N-cadherin	32	27	2	19	12.67	0.000
TGF-β1	42	17	4	17	17.23	0.000
Twist	44	15	2	19	26.82	0.000

Table 2
Correlations of E-cadherin, TGF-β1, N-cadherin and Twist expression levels in the prostate cancer tissue and clinical pathological factors.

Pathological factors		n	E-cadherin			N-cadherin			TGF-β1			Twist		
			Positive	x^2	P	Positive	x^2	P	Positive	x^2	P	Positive	x^2	P
Pathological grade	Highly differentiation	18	9		0.027	6		0.035	9		0.009	9		0.007
	Media differentiated	22	7			13			16			16		
	Low differentiated	19	3			13			17			17		
PSA	⩽20 μg/L	21	14	17.74	0.000	6	8.65	0.030	8	17.41	0.000	8	2.76	0.097
	>20 μg/L	38	5			26			34			34		
Clinical stage	A, B stage	26	10	0.83	0.361	10	4.66	0.031	14	6.81	0.009	14	6.99	0.008
	C, D stage	33	9			22			28			28		
Lymphatic metastasis	yes	17	4	0.82	0.364	13	4.76	0.029	16	4.65	0.031	16	6.37	0.012
	no	42	15			19			26			26		
Osseous metastasis	yes	14	3	0.44	0.509	11	4.38	0.036	14	5.72	0.017	14	4.62	0.032
	no	45	16			21			28			28		
Age (Years old)	⩽68	28	6	2.83	0.092	18	2.17	0.141	22	1.41	0.234	22	1.27	0.260
	>68	31	13			14			20			20		

μg/L group (P<0.05). There was no significant difference in Twist expression between serum PSA > 20 μg/L group and serum PSA ⩽ 20 μg/L group (P>0.05; Table 2).

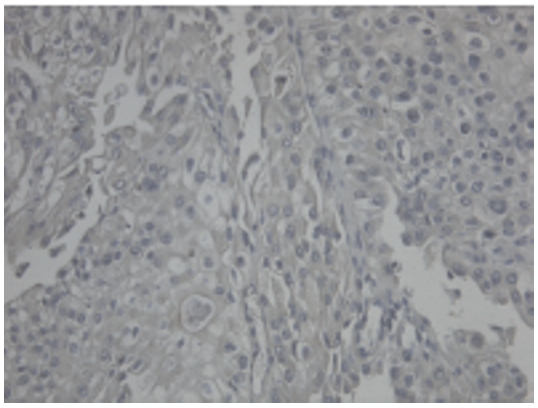

Figure 1. N-cadherin-positive expression in the prostate cancer tissue (SABC, ×400).

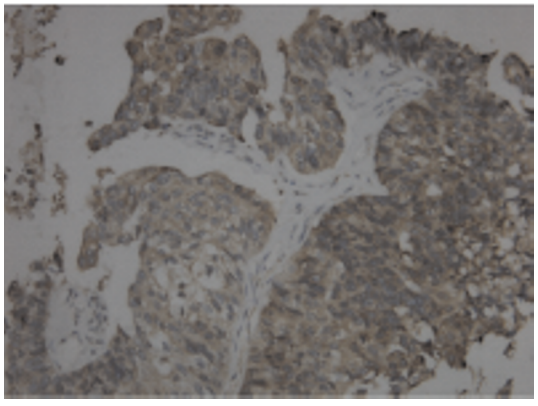

Figure 2. TGF-β1-positive expression in the prostate cancer tissue (SABC, ×400).

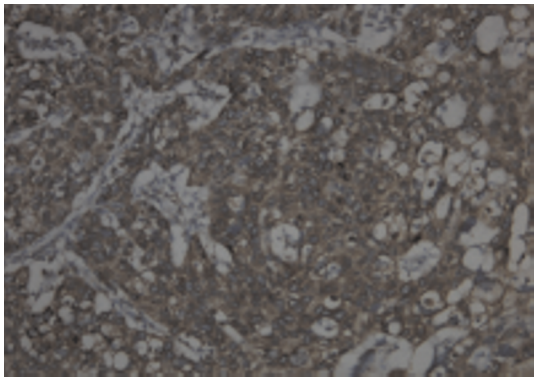

Figure 3. Twist-positive expression in the prostate cancer tissue (SABC, ×400).

3.3. Correlations among E-cadherin, N-cadherin, TGF-β1 and Twist expression in the prostate cancer tissue

Spearman's rank correlation analysis of E-cadherin, N-cadherin, TGF-β1 and Twist expression in the prostate cancer tissue was performed using SPSS 13.0 for windows software. E-cadherin expression was negatively correlated with N-cadherin expression (r=-0.532, P<0.05), Twist expression negatively correlated with E-cadherin expression (r=-0.681, P<0.05), TGF-β1 expression negatively correlated with E-cadherin expression (r=-0.362, P=0.005), and TGF-β1 expression was positively correlated with N-cadherin (r=-0.392, P=0.002) and Twist expression (r=-0.488, P=0.000). However, there was no correlation between Twist and N-cadherin expression (r=-0.245, P=0.061) (Table 3, 4).

Table 3
Correlation of E-cadherin and N-cadherin in the prostate cancer tissue (n).

E-cadherin	N-cadherin		Total
	+	-	
+	3	16	19
-	29	11	40
Total	32	27	59

Table 4
Correlation of Twist and E-cadherin in the prostate cancer tissue (n).

Twist	E-cadherin		Total
	+	-	
+	6	38	44
-	13	2	15
Total	19	40	59

4. Discussion

Human E-cadherin coding gene is located on chromosome 16 at position 22.1, with a protein molecular weight of 120 kD, which contains 723-748 amino acids. Its molecular structure is composed of an intracellular C-end domain, an extracellular N-end domain and a hydrophobic transmembrane domain. The intracellular C-end domain binds to catenin to form functional cadherin-catenin complex, which stabilizes E-cadherin on the cytoskeleton. The extracellular N-end domain identifies and mediates cell-cell adhesion through the His-Ala-Val structure. Down-regulation or loss of E-cadherin expression inevitably decreases the stability between epithelial cells and disturbs cell polarity. For this reason, downregulated E-cadherin expression is considered a marker of the occurrence of EMT. A previous report[7] reported that downregulation of E-cadherin expression in the epithelial tumor tissue is common and correlates with tumor grading. Strong evidence exists that E-cadherin expression basically disappears or is greatly downregulated in poorly differentiated tumor cells, such as breast cancer[8], stomach cancer[9], liver cancer[10] and rectal cancer[11]. Results from this study showed that E-cadherin expression was significantly lower in the prostate cancer tissue than in the adjacent tissue (P<0.05), and it was closely related to the degree of tissue differentiation

(P<0.05) but not related to clinical stage, lymph node or bone metastasis and patient's age (*P*>0.05). At present, the expression and significance of E-cadherin in the prostate cancer tissue remains controversial. The possible mechanism is that in the early stage prostate cancer tissue, downregulated E-cadherin expression inevitably decreases cell-cell stability, leading to desquamation of an increased proportion of local cells and easily resulting in tumor cell infiltration and metastasis; however, after infiltration and metastasis, tumor cells colonize and grew in a new area, during which, E-cadherin expression is needed, and tumor cells likely re-express prior downregulated E-cadherin to promote the growth and expansion of metastatic tumor cells in the newly colonized area. Therefore, E-cadherin expression is different in different developmental periods of prostate cancer. Results from this study also showed that a small number of prostate cancer cells expressed E-cadherin in the cellular membrane, and the expression is largely in the cytoplasm. This occurs possibly because the prostate cancer cell can still synthesize E-cadherin, but the formation of E-cadherin-catenin complex is inhibited, distributing the normal expression of E-cadherin in the cellular membrane. Gottardi *et al*[12] reported that catenin exists in the rectal cancer cells in two forms: one form is to form complex with cadherin and the other form is to bind to T cell factors to activate catenin and inhibit the formation of E-cadherin-catenin complex. However, whether this mechanism is also behind the prostate cancer cells requires further investigation.

N-cadherin, with encoding gene on chromosome 18 at position 11.2 and a protein molecular weight of 127 kD, is only expressed in neuroectodermal and mesodermic tissues, for example, mature muscle, nerve and hemopoietic tissue but hardly expressed in the normal epithelial cells. N-cadherin expression in the epithelial tissue can alter the normal morphology and biological behavior of the epithelial cells and transform epithelial cells into mesenchyme-like cells, *i.e*., the occurrence of EMT. Results from in vitro experiments[13,14] have shown that after successfully transfecting N-cadherin into the cancer cells that do not express N-cadherin, the invasive ability of the cancer cells is significantly increased. In a breast cancer cell experiment, Hazan *et al*[15] found that application of anti-N-cadherin antibody can effectively reduce the migration of breast cancer cells across the vascular endothelium, and compared to low E-cadherin expression, high N-cadherin expression more directly promotes the progression of EMT. A previous study[16] reported that N-cadherin can help cancer cells to escape from the primary foci and promote cancer cells to adhere to extracellular matrix or endothelium, playing an important role in the infiltration and metastasis of tumor cells. Gwak *et al*[17] found that N-cadherin resists the apoptosis of tumor cells and thereby participates in tumor progression. The above findings suggest that N-cadherin is closely related to tumor cell infiltration and metastasis and pathological grades. In this study, we detected N-cadherin expression in the prostate cancer tissue and adjacent tissue at different developmental periods of prostate cancer and our results are consistent with above findings. Our results also showed that both E-cadherin and N-cadherin expression is related to serum PSA level. When serum PSA level is > 20 μg/L, E-cadherin expression is decreased while N-cadherin expression is increased. Serum PSA is an important index of detecting prostate cancer and patients with higher level of serum PSA exhibit poorer prognosis than patients with lower level of serum PSA[18]. We considered that decreased E-cadherin expression and abnormal N-cadherin expression decrease cell-cell adhesion, destroy cell morphology and integrity, and alter prostate cell permeability, which may contribute to the increase in serum PSA level, further revealing that these changes are related to the occurrence of prostate cancer.

E-cadherin and N-cadherin are typical cadherins, but these two exert opposite roles during the metastasis of tumor cells. The precise mechanism has not been fully understood. Hazan *et al*[19] proposed the hypothesis "cadherin switch" and considered that "cadherin switch" is one of important mechanisms underlying EMT. "Cadherin switch" refers to cadherin transformation from type E to type N during normal cell transformation into malignant cells. Results from this study have demonstrated that with the decrease in the degree of differentiation of prostate cancer cells, E-cadherin expression is significantly decreased while N-cadherin expression is significantly increased (*P*<0.05). Spearman's rank correlation analysis results showed that E-cadherin expression was highly negatively correlated with N-cadherin expression, indicating that the cadherin indeed switches from E-cadherin to N-cadherin in prostate cancer.

TGF-β can inactivate macrophages by directly inhibiting the formation of reactive oxygen and the intermediate products and indirectly antagonizing the effects of tumor necrosis factor-γ and tumor necrosis factor-α on macrophages. Reactive oxygen and the intermediate products exhibit very important role in the immunological function of macrophages and can be upregulated by tumor necrosis factor-γ and tumor necrosis factor-α. TGF-β regulates T cell immunologic response by inhibiting the proliferation and function of lymphocytes. TGF-β better inhibits the proliferation of mature or activated T cells and it mainly inhibits anti-CD3 antibody or mitogen-activated T cells by downregulating interleukin-2 expression. TGF-β can increase the sensitivity to apoptosis of T cells activated in the early stage and induce the growth retardation of T cells and the accumulation of G1 stage cells. TGF-β can downregulate the expression of human leukocyte antigen-DR, decrease the expression of interleukin-1 and tumor

necrosis factor-α in monocytes and simultaneously decrease the expression of interleukin-1 receptor and interleukin-1 receptor antagonist. TGF-β can inhibit the formation of tumor necrosis factor-γ generated by the T cells stimulated. Therefore, TGF-β is considered to have obvious double-sided effects in the occurrence and development of tumors. TGF-β1, an important member of TGF-β superfamily, can promote the infiltration and metastasis of tumor cells, but the precise mechanism has not been fully clarified. A previous study regarding pancreatic cancer cells[20] reported that TGF-β1 promotes N-cadherin expression but it inhibits E-cadherin expression. Results from this study showed that TGF-β1 expression was significantly higher in the prostate cancer tissue than in the adjacent tissue; TGF-β1 expression was increased with decrease in degree of differentiation of tumor cells, increase in clinical stage, and lymph node or bone metastasis; moreover, TGF-β1 expression was positively correlated with N-cadherin expression and negatively correlated with E-cadherin. In addition, the present results also showed that TGF-β1 expression was increased when serum PSA level was > 20 μg/L. TGF-β1 can stimulate osteoblasts and promote bone metastasis, and there is an increased risk of bone metastasis when serum PSA level is 20 μg/L[21]. In this study, serum PSA level > 20 μg/L appeared in 14 patients and TGF-β1 expression was all positive, so serum PSA level > 20 μg/L was a possible marker of bone metastasis. Taken together, TGF-β1 exhibits a promoting effect in the occurrence of prostate cancer and subsequent infiltration and metastasis of tumor cells, indicating that TGF-β1 can be taken as an important index of determining the progression and prognosis of prostate cancer.

Recently, great importance has been continuously attached to EMT in the infiltration and metastasis of tumor cells and Twist has been a new exciting field. Twist is generally acknowledged to be an oncogene protein. It directly inhibits E-cadherin expression by regulating E-box in the E-cadherin promoter region and thereby induces the occurrence of EMT[22]. Evidence exists that TGF-β participates in Twist promotion of EMT via PI3K/AKT pathway, RAS/MAPK pathway and SAMD pathway. Therefore, Twist likely plays a central action in the process of EMT. Previous studies have demonstrated that Twist is highly expressed in various tumors, such as breast cancer[23], nasopharyngeal cancer[24], bladder cancer[25] and melanoma[26]. The mechanisms by which Twist promotes the occurrence and development of tumors are as follows: Twist starts EMT, inhibits cell apoptosis via encoding inhibitor of apoptosis protein, interferes P53 pathway, inhibits P21 gene and promotes tumor angiogenesis. Yang *et al*[27] found that Twist is highly expressed during the process of metastasis of tumor cells and plays an important role in intravascular infiltration and distal metastasis of cancer cells and that getting rid of Twist expression by RNA interference technology greatly decreases the velocity of cancer cells entering into the blood circulation and the number of cancer cells that transfer to the lung. Immunohistochemical detection results from this study showed that Twist was highly expressed in the prostate cancer tissue and the expression difference was statistically significant under different clinical pathological factors related to prostate cancer, in terms of the degree of tissue differentiation, clinical stage, lymph node metastasis, and bone metastasis; Spearman's rank correlation results showed that Twist expression was highly negatively correlated with E-cadherin expression and TGF-β1 expression was highly positively correlated with Twist expression. The present results are consistent with above-mentioned viewpoint. Our results suggest that high Twist expression indicates the malignant metastasis of tumor cells and is one of signals for poor prognosis. Because Twist expression is closely related to the pathological factors of prostate cancer, so if Twist can be used for gene diagnosis, then this technique will be of important significance in enhancing the diagnostic accuracy of prostate cancer and determining the prognosis. Twist can be used as a target of tumor biotherapy, and inhibiting or getting rid of Twist expression using biological targeted therapy can achieve the purpose of prostate cancer treatment, providing a new thought and pathway for the diagnosis and treatment of prostate cancer.

The incidence and development of prostate cancer is a multi-step and multi-stage complex process. The decrease in adhesion between tumor cells is the first step of tumor cell infiltration and metastasis, and EMT contributes to this step. EMT is initially recognized during the process of embryonic development and organ formation, and it is generally accepted that tumor cells infiltrate and transfer by simulating this process. Some scholars[28] found that the incidence and development of prostate cancer are similar to the development of embryonic prostate gland and proposed a concept that prostate cancer re-starts the development of prostate gland. The pathological process of tumor cell infiltration and metastasis is closely related to EMT in prostate cancer. Abnormal expression of E-cadherin and N-cadherin is the most important molecular event in prostate cancer, and TGF-β1and Twist play an important regulatory role in this process. However, the underlying molecular mechanism remains poorly understood and whether many more signal molecules participate in the regulation needs to be further investigated.

Conflict of interest statement

We declare that we have no conflict of interest.

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