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Original Article

Nucleus DJ-1/Park7 acts as a favorable prognostic factor and involves mucin secretion in invasive breast carcinoma in Chinese population

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Abstract: Background: DJ-1/Park7 is a cancer- and Parkinson's disease-associated protein which has been implicated in various aspects of malignant transformation in human tumors. The aim of this study was to evaluate the relationship between nuclear DJ-1/Park7 expression by immunohistochemistry and clinicopathologic parameters in invasive breast carcinomas in Chinese population. Methods: We assessed 258 cases of invasive breast carcinomas using formalin fixed, paraffin embedded tissues, including invasive ductal carcinoma-not otherwise specified (IDC-NOS) and special types. Results: We found that nuclear DJ-1/Park7 expression in various invasive breast carcinomas were obviously down-regulated than that in normal mammary gland, only except that in mucinous carcinoma. Increased nuclear expression of DJ-1/Park7 was correlated with some clinicopathologic parameters which were indicators of better prognosis, such as better histological grade, lower Ki-67 index, higher ER/PR expression while decreased nuclear location was associated with triple and HER2 negativity. Furthermore, we expanded to mucinous adenocarcinoma and signet-ring cell carcinoma from stomach, colorectum and lung. Interestingly, nuclear expression of DJ-1/Park7 in mucinous carcinoma from different organs had a similar fold higher than that in adjacent normal gland and the nuclear expression level in signet-ring cell carcinoma were intermediate between corresponding normal gland and mucinous carcinoma. Conclusions: We hypothesized that nuclear location of DJ-1/Park7 might indicate favorable prognosis for patients with invasive breast carcinoma and play a potential role in mucin secretion in adenocarcinomas.

Keywords: DJ-1/Park7, nuclear expression, invasive breast carcinomas, Chinese population, mucin secretion, prognosis

Introduction

Breast cancer, one of the most common malignancies, is a growing heath problem in Asian country [1]. It has been the most frequent cancer of woman and the first great cause of the woman cancer mortality [2]. Identification of diagnostic and prognostic biomarker for breast carcinoma might help to early diagnosis and increase survivability of patients.

DJ-1/Park7 has been reported as an oncogene that can transform mouse NIH-3T3 cells in cooperating with other oncogenes such as H-Ras [3]. DJ-1, also known as Park7 (Parkinson disease (autosomal recessive, early onset) 7) is a member of the peptidase C56 family of proteins. Accumulating evidences have shown that DJ-1/Park7 has been implicated in tumor differentiation [4], invasion and metastasis [5, 6]. DJ-1/Park7 protein was demonstrated ubiquitous expression in both cytoplasm and nucleus [7] and transferred from cell to serum or excretion when cellular oncogenesis [8, 9].

It has been generally recognized that DJ-1/Park7 is over-expressed and secreted in certain types of malignancy such as non-small cell lung carcinoma [10], cervical cancer [11] and pancreatic cancer [12], and over-expression of DJ-1/Park7 was correlated with poorer clinical outcome and lower survival rates. Yet only few studies reported the significance of nucleus DJ-1/Park7 expression in tumor. Yuen [13] et al

Table 1. Relationship between clinicopathological characteristics and DJ-1/Park7 expression in patients with invasive breast carcinomas

Parameter	DJ-1/Park7 nuclear expression (mean)	*P* value (spearman)
BMI[#] index		0.504
< 18.50	0.74	
18.50-24.99	1.37	
≥ 25.00	1.14	
Location		0.760
Left	1.23	
Right	1.41	
Both	1.00	
P53		0.036*
0-30%	1.391	
> 30%	1.197	
ER		0.001*
0	0.781	
< 10%	0.876	
10-50%	1.814	
> 50%	1.627	
PR		0.005*
0	0.870	
< 10%	1.423	
10-50%	1.179	
> 50%	1.869	
HER2		0.691
0	1.125	
1+	1.795	
2+	1.272	
3+	0.973	
Ki-67		0.002*
< 14%	1.583	
≥ 14%	0.922	
T stage		0.203
T1	1.518	
T2	1.130	
T3	1.207	
T4	1.339	
Histological grade		0.002*
I	2.509	
II	1.430	
III	1.077	
Lymph node metastasis		0.514
Negative	1.415	
Positive	1.202	
Intrinsic subtype		0.015*
Luminal A	1.783	
Luminal B	1.204	
HER2[##]	0.735	
TN[###]	0.723	

[#]BMI, body mass index (normal wright: 18.50-24.99; overweight ≥ 25.00; underweight < 18.50), [##]HER2, Her2 positive (non luminal) subtype, [###]TN, triple negative subtype. *P < 0.05.

demonstrated DJ-1/Park7 of cell nucleus played an important role in progression of tumor in esophageal squamous cell carcinoma and Miyajima [14] et al reported that nuclear status of DJ-1/Park7 had a significant association with WHO grading and clinical outcome of patients in astrocytomas. DJ-1/Park7 would translocated from cytosolic pool to nucleus in response to oxidative stress with physiologically active of dimerization [15]. And in the research of fundamentally function, DJ-1/Park7 within the nucleus are reported to be involved in processes of cell death and signal-regulating kinase 1 activity [16]. The role of nucleus DJ-1/Park7 on prognosis in breast cancer remains unknown.

Previous studies demonstrated that DJ-1/Park7 was secreted into serum [17] and nipple fluid [18] and low expression of DJ-1/Park7 protein was predictive of poor outcome in patients with invasive ductal carcinoma (IDC) [19]. However, the expression of nucleus DJ-1/Park7 in invasive breast carcinoma of special type is still unclear. Present study aims to investigate the significance of nucleus DJ-1/Park7 expression as well as the relationship between that and clinicopathologic parameters in Chinese patients with various invasive breast carcinomas, including invasive ductal carcinoma (IDC), pure mucinous carcinoma (PMC), invasive lobular carcinoma (ILC) and invasive micropapillary carcinoma (IMPCa).

Materials and methods

Patients and specimens

All the specimens were collected in Department of Pathology, Union Hospital, Tongji Medical College, Huazhong University of Science and Technology during January 2011 to December 2013. The specimens of surgical material were collected from 258 patients with invasive breast carcinoma, including invasive ductal carcinoma (IDC, 153 cases), pure mucinous carcinoma (PMC, 41 cases), invasive lobular carcinoma (ILC, 33 cases), and invasive micropapillary carcinoma (IMPCa, 31 cases). Patients aged between 34 and 80 years (median 45 years) had undergone modified radical mastectomy. Furthermore, to investigate the expression pattern of DJ-1/Park7 in mucinous car-

Table 2. Clinical features of patients with mucinous adenocarcinoma

Clinical variables	Colorectum	Stomach	Lung
Age			
Average (range)	51 (29-77)	60 (47-79)	52 (36-63)
Gender			
Male	10 (55.6%)	15 (88.2%)	5 (38.5%)
Female	8 (44.4%)	2 (11.8%)	8 (61.5%)
Location			
	Ileocecum 3 (16.7%)	Distal stomach 7 (41.2%)	Left upper lobe 4 (30.8%)
	Ascending colon 5 (27.8%)	Cardia 3 (17.6%)	Left lower lobe 3 (23.1%)
	Transverse colon 2 (11.1%)	Gastroesophageal junction 2 (11.8%)	Right upper lobe 2 (15.4%)
	Rectum 7 (38.9%)	Remnant stomach 2 (11.8%)	Right-middle lobe 1 (7.7%)
	Anal canal 1 (5.5%)	Pylorus 2 (11.8%)	Right lower lobe 3 (23.1%)
		Unknown 1 (5.9%)	
Tumor size			
T1	1 (5.55%)	0	8 (61.5%)
T2	2 (11.1%)	1 (5.9%)	3 (23.1%)
T3	14 (77.8%)	3 (17.6%)	1 (7.7%)
T4	1 (5.55%)	13 (76.5%)	1 (7.7%)
Nodal state			
N0	3 (16.7%)	1 (5.9%)	6 (46.1%)
N1	15 (83.3%)	12 (70.6%)	3 (23.1%)
N2	0	3 (17.7%)	4 (30.8%)
N3	0	1 (5.9%)	0
Clinical stage			
I	1 (5.55%)	0	6 (46.1%)
II	2 (11.1%)	3 (17.7%)	2 (15.4%)
III	14 (77.8%)	13 (76.5%)	5 (38.5%)
IV	1 (5.55%)	1 (5.9%)	0

cinoma from different organs, primary mucinous adenocarcinoma of stomach (17 cases), colorectum (18 cases), lung (13 cases) and primary signet-ring cell carcinoma (SRCC) of stomach (14 cases), colorectum (13 cases) and lung (2 cases) were also employed. All the cases were histologically diagnosed according to the World Health Organization classification of tumors [20]. The patients in present study had no chemotherapy or radiotherapy prior resection. All the clinical data were obtained through review of the patients' medical records. The clinical and pathological characteristics of those patients are listed in **Tables 1** and **2**. The histological grade of IDC was classified according to the Nottingham/Tenovus Primary Breast Cancer Study [21]. The study was approved by the Ethics Committee of Tongji Medical College, Huazhong University of Science and Technology. As this was a retrospective study using archived tissue specimens, the Institutional Ethics Committee waived the need for written informed consent.

Immunohistochemical staining

All the specimens were fixed in 10% neutral formalin and then paraffin-embedded for routine histopathology. After removing paraffin and hydration, the paraffin sections (4 μm) were blocked endogenous peroxidase activity with 3% hydrogen peroxide at room temperature (RT) for 5 min. The antigen was then retrieved in 0.01 mol/L sodium citrate buffer at PH 6.0 and heated by autoclaving for 15 s. After cooling to RT and rinsing in phosphate-buffered saline (PBS) for 5 min by 3 times, the sections were blocked with non-immune rabbit serum at RT for 15 min. Then DJ-1/Park7 primary antibody (rabbit monoclonal antibody, NBP1-40495, Novus Biologicals, Littleton, USA) was used at a dilution of 1:5500 and incubated at

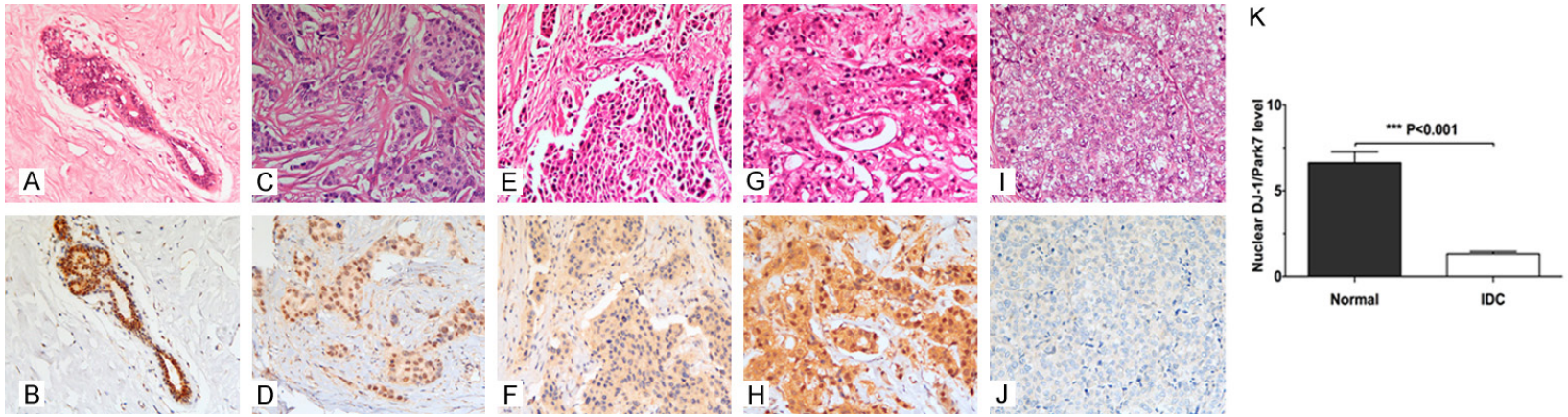

Figure 1. Histologic and immunohistochemical features for DJ-1/Park7 protein expression in normal mammary gland (A, B) and invasive ductal carcinoma (IDC) (C-J, original magnification × 200). Immunohistochemical staining of DJ-1/Park7 presents a different intensity of nuclear and cytoplasmic reaction. Normal mammary gland (A for H&E, B for IHC staining) shows high DJ-1/Park7 protein expression; Strong staining of DJ-1/Park7 in nucleus of IDC tissues (C for H&E, D for IHC staining); Strong staining of DJ-1/Park7 in cytoplasm of IDC tissues (E for H&E, F for IHC staining); Strong staining of DJ-1/Park7 in both nucleus and cytoplasm of IDC tissues (G for H&E, H for IHC staining); Weak staining of DJ-1/Park7 in both nucleus and cytoplasm of IDC tissues (I for H&E, J for IHC staining); Nuclear DJ-1/Park7 expression was significantly lower in invasive ductal carcinoma compared with that in normal breast ductal epithelium (K).

37°C for 1 h. ER (SP1, ready-to-use), PR (1E2, ready-to-use) and Her-2 (4B5, ready-to-use) from *Roche Diagnostics Gmbh (Shanghai, China)* were stained according to the supplied instruction manual. Ki-67 (*SP6, Gene Tech Company Limited, Shanghai, China*) and P53 *(D07, Gene Tech Company Limited, Shanghai, China*) were applied 1:100 dilution for overnight at 4°C. Afterward, the sections were subsequently incubated with anti-rabbit secondary antibody (SM802, Dako, Shanghai, China) at 37°C for 30 min. After coloring with 3, 3'-diaminobenzidine (DAB) at RT for 15 min and counterstaining with hematoxylin, insoluble brown products conjugated with DJ-1/Park7 antigen can be revealed under the microscope.

Evaluation of immunohistochemical staining results

Immunohistochemical staining results were evaluated by two independent pathologists (D.Y. and Y.L.) who had no advanced awareness about clinicopathologic data of patients. The choice of specimens for the evaluation was completely arbitrary. Cancer cells should be regarded as positive when it showed granular brown staining. Normal breast duct epithelium expressed DJ-1/Park7 in cytoplasm and nucleus as an internal control of DJ-1/Park7. Assessment of immunohistochemical expression on nucleus DJ-1/Park7 was performed by light microscopy at × 400 magnification. Thirty microscopic fields which included at least 50 cancer cells were randomly selected. We evaluated the average of positive nuclear staining numbers in thirty fields, after counting at least 1,000 tumor cells. The evaluation of HER-2 was assessed according to the ASCO/CAP (2013) system [22]. The positivity of ER and PR were considered as ≥ 1% tumor cells with nuclear staining [23]. The Ki-67 and P53 labelling index (LI) (%) were evaluated by counting the percentage of positively cancerous cells which was prominent stained of nuclei in a high-power field (400 ×). Breast cancer was separated into four subtypes [24]: luminal A (ER+/PR+, HER2-, Ki-67 < 14%), luminal B (ER+/PR+, HER2-, Ki-67 ≥ 14%) or (ER+/PR+, HER2+), HER2 positive (ER-, PR-, and HER2+) and triple-negative (ER-, PR-, and HER2-).

Statistical analysis

The data were analyzed by using the SPSS version 19.0 statistical program for windows (SPSS, Inc., Chicago, IL, USA). The spearman rank test, Mann-Whitney U, and Fisher's exact test were employed. A two-tailed $P < 0.05$ was considered as statistically significant.

Results

Nucleus DJ-1/Park7 expression in invasive ductal carcinoma and adjacent normal breast ductal epithelium

Positive staining for DJ-1/Park7 protein was characterized by intense cytoplasmic and nuclear reactivity in normal breast ductal epithelium (**Figure 1A**, **1B**). Yet the cancer cells exhibited either nuclear expression alone (**Figure 1C**, **1D**) or cytoplasmic expression alone (**Figure 1E**, **1F**) or combinative expressions (**Figure 1G**, **1H**) or complete negativity (**Figure 1I**, **1J**) for DJ-1/Park7. The majority of cancer cells (59.2%) demonstrated both cytoplasmic and nuclear reactivity like normal breast ductal epithelium. Nuclear DJ-1/Park7 expression was significantly lower in invasive ductal carcinoma compared with that in normal breast ductal epithelium (**Figure 1K**, normal vs tumor: mean ± SE = 6.628±0.682 vs 1.314± 1.700, $P < 0.05$, Mann-Whitney U = 121.500). Nuclear expression level of the protein varied from case to case and seemed to be associated with clinicopathological parameters which would be illustrated in details below.

Nucleus DJ-1/Park7 expression in invasive breast carcinoma of special type

To further demonstrate the nuclear expression of DJ-1/Park7 in invasive breast carcinoma of special type, we further investigated that in ILC (**Figure 2A**, **2B**), PMC (**Figure 2C**, **2D**) and IMPCa (**Figure 2E**, **2F**). The nuclear DJ-1/Park7 expression varied among histology types. The means (range) of nuclear DJ-1/Park7 in patients with ILC, PMC and IMPCa were 3.59 (0.167-11.467), 7.66 (0.130-32.530), 3.48 (0.030-10.730), respectively (**Figure 2G**). Furthermore, the nuclear expression of DJ-1/Park7 in ILC ($P < 0.001$, Mann-Whitney U = 102.00) and IMPCa ($P < 0.001$, Mann-Whitney U = 106.00), except that in pure mucinous carcinoma, were notably lower compared to that in normal breast ductal epithelium (6.628±0.682).

Correlations between nucleus DJ-1/Park7 expression and clinicopathological parameters in patients with invasive breast carcinoma

Stronger nucleus DJ-1/Park7 expression was remarkably correlated with higher expression

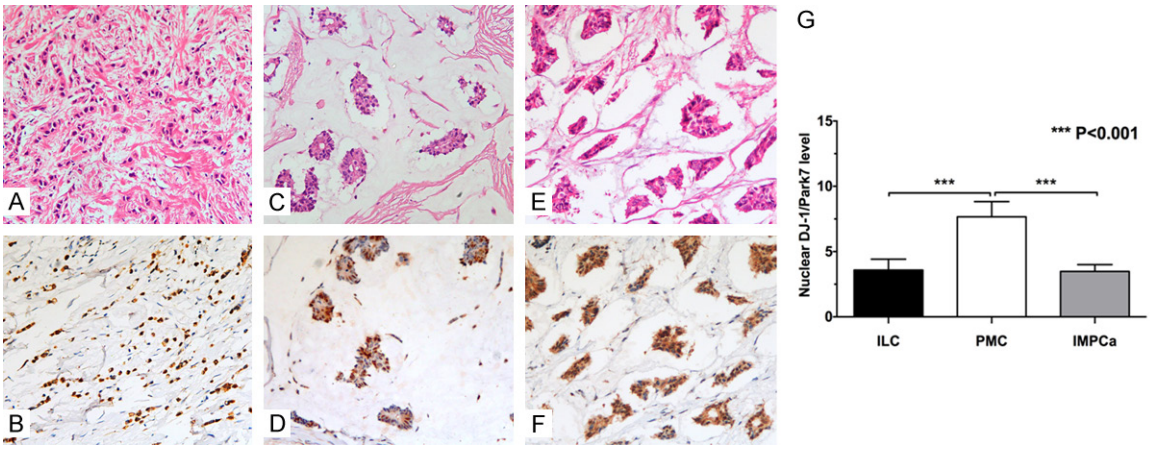

Figure 2. Representative images DJ-1/Park7 expression in invasive breast carcinomas of special type (original magnification × 200). Invasive lobular carcinoma (ILC) (A for H&E, B for IHC staining); pure mucinous carcinoma (PMC) (C for H&E, D for IHC staining); invasive micro-papillary carcinoma (IMPCa) (E for H&E, F for IHC staining); (G) Summary of nucleus DJ-1/Park7 expressions in different invasive breast carcinomas.

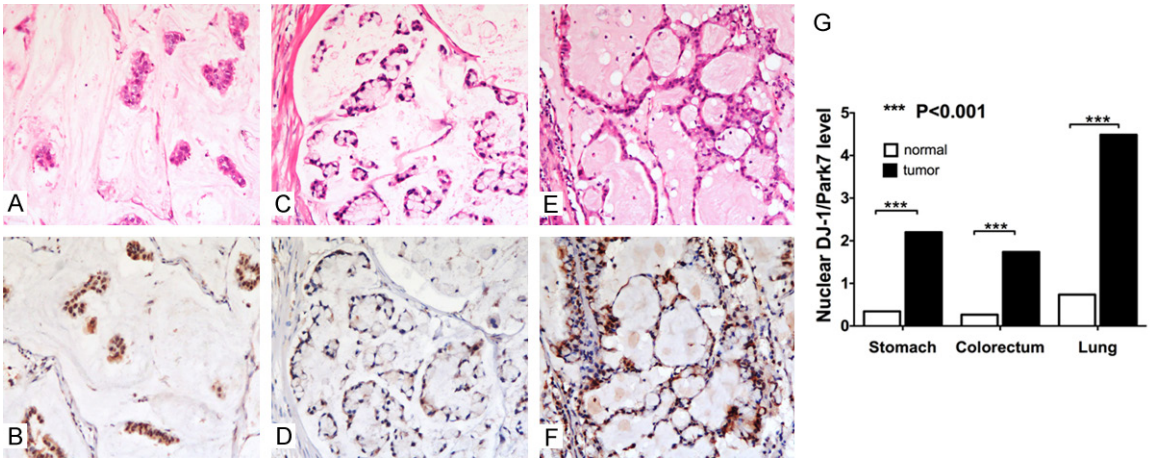

Figure 3. Representative images of DJ-1/Park7 expression in mucinous carcinoma of stomach (A for H&E, B for IHC staining), colorectum (C for H&E, D for IHC staining) and lung (E for H&E, F for IHC staining) (original magnification × 200). (G) Summary of nucleus DJ-1/Park7 expressions in mucinous carcinomas from different organs.

of ER and PR, better histological grade, lower expression of P53 and Ki-67. Different nuclear expression of DJ-1/Park7 were also demonstrated diversely between intrinsic subtypes of invasive breast carcinoma. Nuclear expression of DJ-1/Park7 in luminal A were apparently higher than that in HER-2 positive and triple negative subtypes (mean: luminal A = 1.783, HER-2 positive = 0.735, triple negative = 0.723, $P < 0.05$). Yet, nuclear DJ-1/Park7 had no statistical relevance to other clinicopathological parameters, such as BMI, tumor location, HER-2 expression, tumor stage (T) and lymph node metastasis. The details were summarized in **Table 1**.

Nuclear DJ-1/Park7 expression in mucin-producing carcinomas from stomach, colorectum and lung

Since nuclear DJ-1/Park7 expression was down-regulated in most subtypes of invasion breast carcinomas excepted that in pure mucinous carcinoma, we subsequently expanded our immuno-histochemical assessment to primary mucinous carcinoma from stomach (**Figure 3A**, **3B**), colorectum (**Figure 3C**, **3D**) and lung (**Figure 3E**, **3F**). As presented in **Figure 3G**, the nuclear expression of DJ-1/Park7 in mucinous carcinoma was significant higher than that in paired adjacent normal gland (tumor *vs*

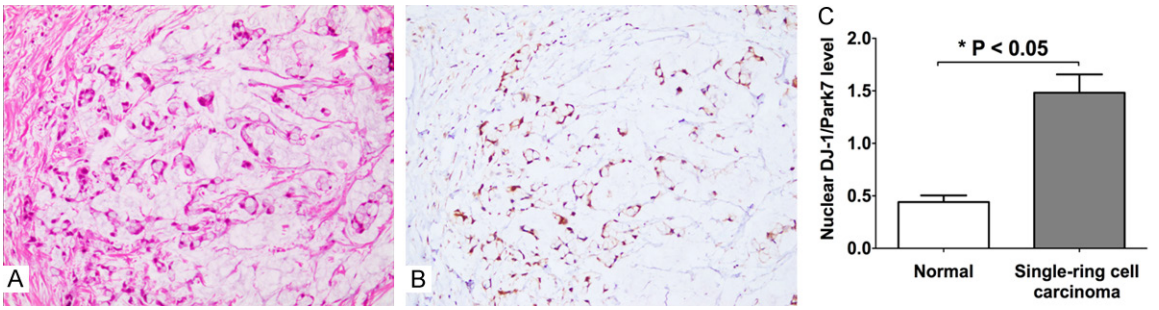

Figure 4. Representative images of DJ-1/Park7 expression in signet-ring cell carcinoma (original magnification × 200). (A) for H&E, (B) for IHC staining of DJ-1/Park7 protein. (C) Summary of nucleus DJ-1/Park7 expressions in normal tissues and signet-ring cell carcinoma.

normal: stomach, 2.200 *vs* 0.344; colorectum, 1.738 *vs* 0.266; lung, 4.490 *vs* 0.736, $P < 0.001$). Interestingly, nuclear DJ-1/Park7 expression in mucinous carcinoma was always 6-fold higher than that in adjacent normal gland, regardless of its histological origin. The clinical characteristics of the patients with mucinous carcinoma were presented and summarized in **Table 2**.

To determine the status of nuclear DJ-1/Park7 expression in mucin-producing but non-secreting adenocarcinoma, we evaluated nuclear expression mode of DJ-1/Park7 in signet-ring cell carcinoma. The nuclear level of DJ-1/Park7 in signet-ring cell carcinoma (**Figure 4A**, **4B**) (mean: stomach 1.33, colorectum 1.63 and lung 1.45) was higher than that in corresponding normal gland yet lower than mucinous carcinoma of the same organ ($P < 0.05$, **Figure 4C**).

Discussion

We have implemented an immunohistochemical process to identify the expression pattern of DJ-1/Park7 and to explore the prognostic significance of nuclear DJ-1/Park7 expression in invasive breast carcinoma. In our research, nuclear DJ-1/Park7 expression was obviously decreased in most subtypes of invasion breast carcinoma compared to that in normal mammary gland except in mucinous carcinoma and nucleus expression of DJ-1/Park7 was negatively correlated with P53, Ki-67 expression and histological grade, positively related with ER and PR expression. Our findings were also supported by the researches from Oda [18] *et al* and Kawate [25] *et al*. In our expanded research, the nuclear expression of DJ-1/Park7 in mucinous carcinoma from different organs had a similar fold higher than that in adjacent normal gland and the nuclear expression in signet-ring cell carcinoma were intermediate between corresponding normal gland and mucinous carcinoma, which were not previously reported as far as we knew.

Like previous reports, Ki-67, ER, PR and P53 have been used as frequently-used prognostic markers in breast cancer. Ki-67 [26] and P53 [27] are indicators of poor prognosis; ER and PR-positive [28] patients indicate relatively good outcomes. The increased expression of mutant p53 was detected in cancer cells, and it might play a role in the tumor progression of invasive breast cancer [27]. Above immunohistochemistry indexes were significant predictors of survival time and outcome in the patients of breast cancer. In our research, nucleus expression of DJ-1/Park7 was negatively correlated with P53, Ki-67 expression and histological grade, positively related with ER and PR expression in invasion ductal carcinoma. Collectively, several lines of evidence illustrated that nucleus DJ-1/Park7 expression played an important role as potential tumor suppressor and negative regulator of neoplasia in invasive breast carcinoma which were consistent with our findings.

DJ-1/Park7 was mainly reported as an oncogene and frequently over-expressed in majority kinds of tumor. The experiment in esophageal squamous cell carcinoma [13] indicated that patients with nuclear DJ-1/Park7 over-expression had poorer patient survival, which suggests that DJ-1/Park7 nuclear expression was significantly associated with Daxx expression in nucleus. Conversely, there were several researches gradually providing evidences about

decreased expression of DJ-1/Park7 protein in different types of tumor. As reported in the research of hepatocellular carcinomas (HCC) [29], DJ-1/Park7 expression in hepatitis B virus-infected, well-differentiated HCC was down-regulated compared to that in adjacent non-tumor tissue. Similarly, in astrocytoma [14], DJ-1/Park7 nuclear expression was inversely correlated with WHO grade of astrocytoma and might play an important role as tumor suppressor. The contradicting conclusions on roles of DJ-1/Park7 protein among various types of carcinomas might be due to the inconsistent evaluation standards from different groups as well as the different isoforms of DJ-1/Park7 involved in multiple cellular processes.

Previous genetic study demonstrated that DJ-1/Park7 was implicated in biological processes of antioxidant stress which played a crucial role in origin, promotion and progression of cancer [30]. Reactive oxygen species (ROS) could promote malignant transformation and cancer progression [31] through accelerating DNA lesion. Previous studies reported that DJ-1/Park7 was mainly localized in the cytosol under normal conditions and translocated from cytoplasm to nucleus [3, 32] or mitochondria [15, 33] by the stimulation of oxidative stress including UV irradiation, H_2O_2, and so on. In response to oxidative stress, DJ-1/Park7 protein translocate to mitochondria within 3 hr and subsequently to nucleus by 12 hr to protect cell against oxidative stress [15]. We speculated that nuclear DJ-1/Park7 in invasive breast carcinoma might play a potential role in tumor suppression by antioxidant stress which therefore served as a good prognostic biomarker.

In our immunohistochemistry-based study, nuclear DJ-1/Park7 status in invasive breast carcinoma was obviously attenuated compared to that in normal mammary gland and DJ-1/Park7 might serve as good prognostic biomarker for patients of invasive breast carcinoma. This hypothesis was supported by the research of Tsuchiya [19] *et al*, who demonstrated that cellular DJ-1/Park7 protein in breast carcinoma was lower than that in adjacent non-carcinoma epithelium accompanying with higher intensity of DJ-1/Park7 mRNA expression and Kawate [25] *et al* also demonstrated that lower expression of DJ-1/Park7 protein in cytoplasm was a significant predictor of shorter disease-free survival and poor outcome in breast cancer patients. Yet these studies ignored to further investigate the sub-cellular location of DJ-1/Park7 and they only employed specimens of invasive ductal carcinoma.

However, it was still unclear how the expression of DJ-1/Park7 existed differently between invasive breast carcinoma and other origins of carcinomas. We speculated that the difference of DJ-1/Park7 expression might be caused by the special secretory pattern of DJ-1/Park7 protein in invasive breast carcinomas during the tumor development and progression.

Supportingly, a study in sera from patients with breast cancer [17] showed that DJ-1/Park7 protein was circulating at high level in sera from breast cancer patients accompanying with low intracellular level of the protein in tumor cells, indicated that translocation of DJ-1/Park7 from intracellular to the extracellular environment during tumor development. Another study in nipple fluid of patients with breast cancer by Oda [18] *et al* also found that low expression of DJ-1/Park7 protein in cancer cells, despite high mRNA expression, was significantly correlated with high DJ-1/Park7 protein levels in nipple fluid. We found that DJ-1/Park7 was decreased in most subtypes of invasion breast carcinomas compared with that in normal mammary gland except in mucinous carcinoma. The translocation of DJ-1/Park7 from nucleus to extracellular might lead to reduced cellular expression of that protein in invasion breast cancer which was distinct from overexpression pattern in carcinomas of other origins from previous reports.

Present study is the first attempt to reveal the diversities of nuclear DJ-1/Park7 expression among subtypes of invasive breast carcinoma. Our research further demonstrated that nuclear expression of DJ-1/Park7 were lower than that in adjacent normal gland except that in mucinous carcinoma, which had not been previously published yet. Nucleus DJ-1/Park7 expression in mucinous carcinoma had a similar fold higher than that in adjacent normal tissue regardless of histological origin. Moreover, the nuclear DJ-1/Park7 expression in signet-ring cell carcinoma which produced mucin without secretion was just intermediate between that in the corresponding normal gland and mucinous carcinoma of the same origin. Mucinous adenocarcinoma and signet-ring cell

carcinoma are both mucin-secreting adenocarcinomas. The World Health Organization (WHO) has defined mucinous carcinoma and SRCC as follows. Mucinous adenocarcinoma is that tumor abundant production of extracellular mucin with clusters of tumor cells. Signet-ring cell carcinoma is defined by the presence of > 50% of tumor cells with prominent intracytoplasmic mucin. We hypothesized that secretion of DJ-1/Park7 might be relevant to the secretion of extracellular mucin and participate into the secretion process of mucin.

In summary, the findings of present research demonstrated that nuclear DJ-1/Park7 might serve as a valuable prognosis predictor for breast cancer. Furthermore, nuclear location of DJ-1/Park7 may play a potential role in production of mucin. To evaluate the role of DJ-1/Park7 in mucin secretion, further studies are warranted.

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Disclosure of conflict of interest

None.

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