

# DEK overexpression is predictive of poor prognosis in esophageal squamous cell carcinoma

Huochun Yi<sup>1</sup>, Hongbing Duan<sup>2</sup>, Wensheng Shi<sup>1</sup>, Zhengjin Liu<sup>3</sup>, Yali Liu<sup>2</sup>

<sup>1</sup>Center of Clinical Laboratory, Zhongshan Hospital, School of Medicine, Xiamen University, Xiamen, Fujian, China

<sup>2</sup>Department of Thoracic, Zhongshan Hospital, School of Medicine, Xiamen University, Xiamen, Fujian, China

<sup>3</sup>Department of Pathology, Zhongshan Hospital, School of Medicine, Xiamen University, Xiamen, Fujian, China

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**Corresponding author:**

Yali Liu

Department of Thoracic

Zhongshan Hospital

School of Medicine

Xiamen University

Xiamen, 361004

Fujian, China

E-mail: [elliy@163.com](mailto:elliy@163.com)

## Abstract

**Introduction:** The *DEK* gene encodes a nuclear phosphoprotein which is involved in multiple cell metabolic processes, such as DNA damage repair, mRNA splicing, modifying chromatin structure and transcription regulation. *DEK* has been shown to be overexpressed in various solid human tumors and associated with patient prognosis. In this study, our aim was to investigate *DEK* protein expression and its relationship with clinicopathological parameters and prognosis in esophageal squamous cell carcinoma (ESCC).

**Material and methods:** Tissue samples were collected from 120 routinely diagnosed ESCC patients who underwent surgical resection at the Zhongshan Hospital, Xiamen University in the period from June 2011 to May 2013. The expression of *DEK* was determined by immunohistochemistry.

**Results:** *DEK* protein was ubiquitously distributed in the nucleus of ESCC cells, and its positive rate (71.7%) was significantly higher in cancer samples than those of para-carcinoma (21.4%) or normal esophageal (13.9%) tissues ( $p < 0.001$ ). Similarly, significantly more cells overexpressing *DEK* were found in ESCC tissues (57.5%) in comparison with para-carcinoma samples (11.4%) and normal esophageal mucosa (0%,  $p < 0.001$ ). The *DEK* overexpression rate was significantly different between patients with different tumor-node-metastasis (TNM) stages and differentiation degrees ( $p < 0.001$ ). ESCC cases with elevated *DEK* amounts showed reduced disease-free and 5-year survival rates compared with those expressing low *DEK* amounts ( $p < 0.001$ ). *DEK* overexpression was also confirmed to independently predict prognosis in ESCC ( $HR = 4.121$ , 95% CI: 1.803–9.42,  $p = 0.001$ ).

**Conclusions:** *DEK* expression is positively correlated with reduced survival in ESCC patients. *DEK* has potential to be an independent biomarker in predicting prognosis of ESCC patients.

**Key words:** *DEK*, esophageal squamous cell carcinoma, immunohistochemistry, prognosis.

## Introduction

Esophageal carcinoma represents the sixth major factor responsible for malignancy-related deaths around the world [1, 2]. Esophageal cancer includes the adenocarcinoma (EAC) and squamous cell carcinoma (ESCC) types. The ESCC comprises almost 9 out of 10 cases in China. Although

important advances exist in multimodal therapy of ESCC, prognosis remains poor, with a 5-year survival rate less than 15% [3]. Therefore, identifying reliable diagnostic and prognostic biomarkers of ESCC is critical, as well as elucidating molecular mechanisms participating in esophageal carcinogenesis [4, 5].

*DEK* was initially discovered as one of the parts of the *DEK-nucleoporin 214 (DEK-NUP214)*, also known as *DEK-CAN* fusion gene arising from a (6;9) translocation in a subtype of patients with acute myeloid leukemia (AML) [6]. Apart from being a fusion protein in AML, the *DEK* gene encodes a nuclear phosphoprotein that has been measured in many solid human tumors, such as hepatocellular carcinoma (HCC), lung cancer, bladder cancer, ovarian cancer and colorectal carcinoma [7–11]. Accumulating reports have indicated that *DEK* is involved in multiple cell metabolic processes, such as DNA damage repair, mRNA splicing, modifying chromatin structure and transcription regulation [12–17]. Several studies have also demonstrated that elevated *DEK* levels might accelerate tumorigenesis and neoplastic progression by means of intervention with cell proliferation, apoptosis, senescence, and differentiation [8, 18–22]. Zhou *et al.* reported that up-regulating *DEK* expression levels in A549 lung cancer cell lines could significantly promote cell proliferation, while restricting cell proliferation in *DEK*-depleted cells [8]. Liu *et al.* demonstrated that the silencing of *DEK* had effects on the growth of CaSki cells with blocking the cell cycle in the G0/G1 phase, inhibiting cell proliferation, increasing cell apoptosis and inducing cell senescence [20]. Wise-Draper *et al.* reported that the expression level of *DEK* protein was particularly repressed during keratinocyte differentiation and *DEK* overexpression in organotypic raft cultures was important for hyperplasia induction [22].

A large number of studies indicate that *DEK* is over-expressed in various malignant tumors, associated with tumorigenesis and advances in tumor invasion [7, 23–27]. For instance, researchers performed a comprehensive analysis of *DEK* expression in different melanocytic tumors and found that *DEK* expression was largely positive in malignant lesions, particularly in metastatic cases, while there was negligible *DEK* expression in benign lesions [23]. Javier *et al.* reported that the *DEK* gene was overexpressed in colorectal cancer cell lines, while knock-down of *DEK* in DLD1 and SW620 cell lines reduced cell migration and increased irinotecan-induced apoptosis [24]. Our previous study also demonstrated that mRNA level of *DEK* in the majority of hepatocellular carcinoma (HCC) tissues was approximately

1.8 times that in matched normal hepatic tissues (0.707 vs. 0.391), while the percentage of positive *DEK* expression in HCC tissues was about 2.19 times that rate in normal tissues (87.3% vs. 40.0%) [7]. Other studies have also shown that *DEK* frequently exhibits an increased expression level in various malignant tumors [25–27]. To date, there is only one study investigated the association between *DEK* expression and ESCC, by employing a *DEK* transgenic mouse model, and it found that *DEK* overexpression is capable of promoting ESCC *in vivo* [28]. Therefore, we conducted a hospital-based study to investigate the association between *DEK* expression in ESCC tissue samples, clinicopathologic features and patient survival.

## Material and methods

### Clinical samples

A total of 120 routinely diagnosed ESCC patients who underwent surgical resection at the Zhongshan Hospital, Xiamen University in the period from June 2011 to May 2013 were assessed. All cases were pathologically confirmed to be ESCC for the first time. Patients were excluded if any of the following conditions were met: (1) presence of tumors other than ESCC; (2) received chemotherapy or radiotherapy; (3) inoperable patients; (4) refusal or inability to participate in the investigation because of poor health. Pathological and demographical indexes, i.e. age, gender, tumor size, tumor-node-metastasis (TNM) stage, degree of tissue differentiation and lymph node metastasis (LNM), were obtained from medical records. Disease-free survival (DFS) and 5-year survival data were collected after follow-up. Our research has been approved by the Medical Ethical Committee of the Zhongshan Hospital, Xiamen University (Ethical Approval No. XMZSYKY-2013-045) after reviewing the research protocol and a formal hearing. We ensured that written informed consent from patients was obtained before using samples in this study.

### Immunohistochemical assessment

Immunohistochemical (IHC) assessment was completed with a DAKO LSAB kit (DAKO A/S, Glostrup, Denmark). 4  $\mu$ m sections were submitted to deparaffinization in xylene, and rehydration in decreasing concentrations of ethanol (100%, 95%, 80% and 70%, respectively). Secondly, slides were incubated with 3% H<sub>2</sub>O<sub>2</sub> in methanol for 15 min at room temperature. Subsequently, antigen retrieval was carried out by boiling in 0.01 M sodium citrate buffer (pH 6.0) for 20 min in a microwave. Sections were incubated in 20% normal goat serum for 20 min and were then incubated

with the DEK-specific primary antibody (1 : 50; BD Biosciences, USA) at 4°C overnight according to the instructions. After incubation with biotinylated secondary antibody (ambient conditions, 30 min), samples were treated with streptavidin-peroxidase complex in ambient conditions for 30 min. Between each above-mentioned step, slides were washed with phosphate-buffered saline (PBS) for 5 min. Then, 3,3'-diaminobenzidine and hematoxylin were employed for development and counterstaining, respectively. Furthermore, samples processed without anti-DEK antibodies were employed as a negative control.

The slides were scored separately by two pathologists unaware of clinicopathological records. Firstly, the entire esophageal tumor was analyzed, and 50 randomly selected fields of view were quantitated, with nuclear staining considered to be positive. Briefly, the following scoring system was adopted for IHC staining: '-' (< 5% positive cells), '+' (5–25% positive cells), '++' (26–50% positive cells) and '+++' (> 50% positive cells) [29, 30]. DEK overexpression was reflected by '++' or '+++' score. In survival analyses, DEK expression was classified as low expression ('-' and '+') and high expression ('++' and '+++') [11, 26, 31].

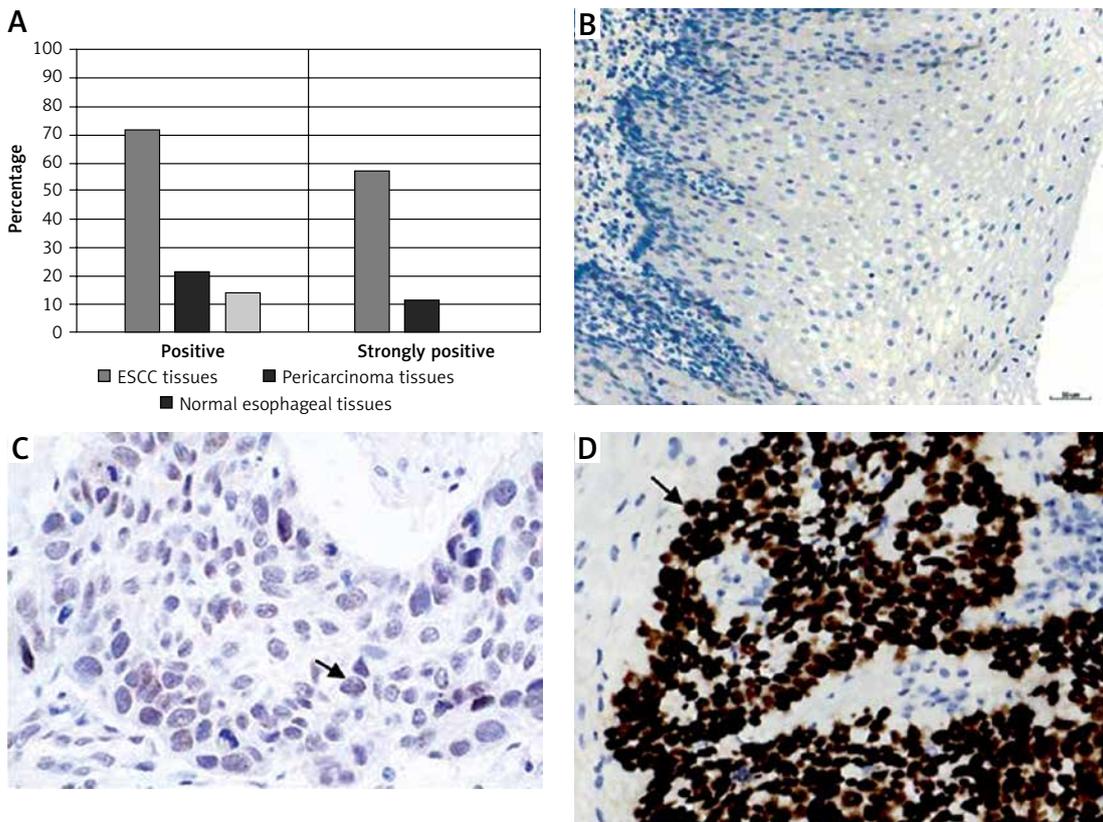
### Statistical analysis

SPSS 18.0 was employed for statistical analyses. Associations of DEK levels with clinicopathological features were assessed by the  $\chi^2$  or Fisher's exact test. Disease-free and 5-year survival rates upon resection were determined by Kaplan-Meier curves and compared by the log rank test. The Cox proportional hazards regression model was employed for multivariate survival analysis of characteristics with statistical significance in univariate analysis. The statistical significance level was set at  $p < 0.05$ .

### Results

#### DEK is highly expressed at the protein level in ESCC

The DEK protein was exclusively found in the nucleus in ESCC tissues by IHC analysis (Figure 1 D). A rate of DEK expression of 71.7% (86/120) was obtained in esophageal cancer tissues, indicating a marked increase compared with the adjacent non-tumor (21.4%, 15/70) and normal esophageal mucosa (13.9%, 5/36) groups. Similarly, the rate of DEK overexpression in ESCC tissues (57.5%,



**Figure 1.** Immunohistochemical detection of DEK in esophageal tissues. **A** – Rates of expression and overexpression of DEK were considerably higher in ESCC in comparison with adjacent noncancerous or normal esophageal mucosal specimens. **B** – DEK protein not found in normal esophageal mucosa (original magnification, 200×). **C** – DEK protein found at low levels in pericarcinoma mucosa (original magnification, 400×). **D** – DEK protein overexpressed in ESCC tissue samples (original magnification, 400×)

69/120) was markedly elevated in comparison with those of the adjacent noncancerous (11.4%, 8/70) and normal esophageal mucosa (0%, 0/36) groups (both  $p < 0.001$ ) (Table I).

**Associations of clinicopathological parameters with DEK protein expression**

The results showed a markedly increased rate of DEK expression in advanced-stage (III–IV) ESCC patients (49/55, 89.1%) compared with the early-stage (I–II) group (20/65, 30.8%) ( $p < 0.001$ ). In addition, an elevated rate of DEK overexpression was found in poorly differentiated esophageal cancers (40/47, 85.1%) compared with moderately and well-differentiated cancers (29/73, 39.7%)

( $p < 0.001$ ). However, DEK overexpression in esophageal cancer showed no associations with age, gender, tumor size or lymph node metastasis ( $p > 0.05$ ) (Table II).

**Association of DEK expression with patient survival in ESCC determined by the Kaplan-Meier method**

The ESCC cases ( $n = 120$ ) were assessed by Kaplan-Meier survival curves. The results indicated that disease-free (log-rank  $p = 0.007$ ) and 5-year (log-rank  $p = 0.008$ ) survival rates were markedly elevated in ESCC patients with reduced DEK amounts compared with those highly expressing this protein (Figure 2).

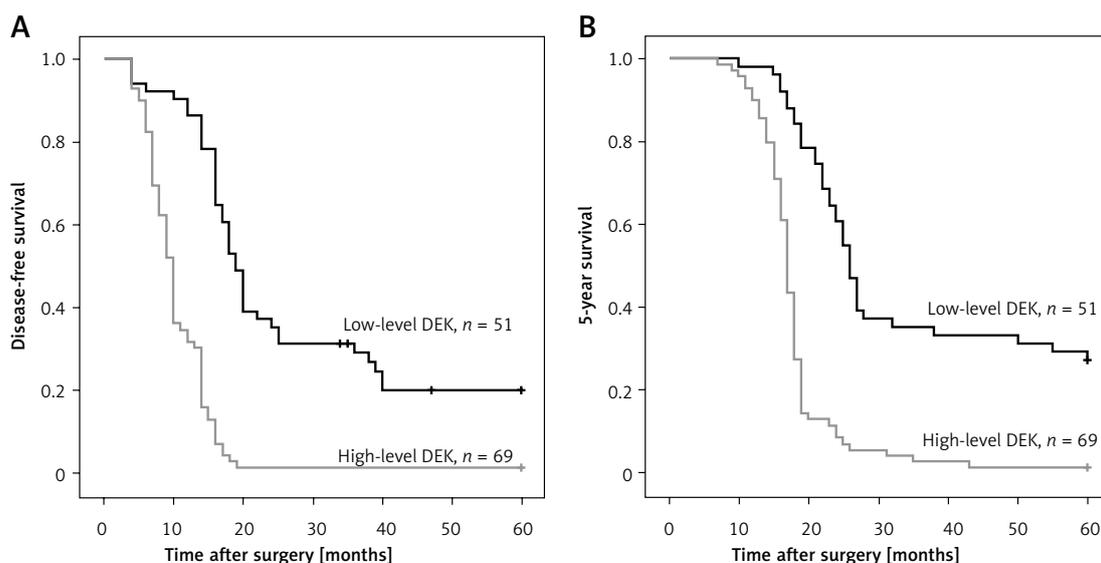
**Table I.** DEK expression level in esophageal tissues

Diagnosis	Number of cases	DEK level				Percentage of expression (%)	Percentage of over-expression (%)
		-	+	++	+++		
Normal esophageal tissues	36	31	5	0	0	13.9	0
Pericarcinoma tissues	70	55	7	8	0	21.4	11.4
ESCC tissues	120	34	17	39	30	71.7*	57.5*

\* $P < 0.001$  (Based on the results of the chi-squared test, the DEK expression rate and overexpression rate of ESCC tissues were significantly higher than the other two groups).

**Table II.** Associations between DEK expression and clinicopathological features of ESCC

Group	Case number	DEK expression		$\chi^2$	P-value
		Low	High		
Gender:				0.209	0.648
Male	85	35	50		
Female	35	16	19		
Age [years]:				0.114	0.736
≤ 60	38	17	21		
> 60	82	34	48		
Tumor size [cm]:				1.841	0.175
≤ 5	72	27	45		
> 5	48	24	24		
TNM stage:				41.467	< 0.001
I + II	65	45	20		
III + IV	55	6	49		
Differentiation degree:				24.095	< 0.001
Low	47	7	40		
Moderate and high	73	44	29		
Lymph node metastasis:				0.768	0.381
No	77	35	42		
Yes	43	16	27		



**Figure 2.** Disease-free and 5-year survival assessment in ESCC patients based on DEK protein amounts. ESCC cases with elevated DEK amounts showed reduced disease-free (A) and 5-year (B) survival rates in comparison with individuals expressing reduced DEK amounts (log-rank  $p < 0.001$ )

**Table III.** Univariate and multivariate analyses by the Cox regression model for ESCC survival

Characteristic	B	SE	Wald	HR	95% CI		P-value
					Lower	Upper	
Univariate analysis:							
Gender	0.402	0.234	2.94	1.495	0.944	2.366	0.086
Age	0.365	0.238	2.364	1.441	0.904	2.296	0.124
Tumor size	0.458	0.235	3.808	1.582	0.998	2.507	0.051
TNM stage	1.224	0.214	32.596	3.399	2.233	5.174	< 0.001**
Differentiation degree	0.91	0.38	5.741	2.484	1.18	5.229	0.017*
Lymph node metastasis	1.594	0.24	44.166	4.925	3.078	7.883	< 0.001**
DEK	1.375	0.22	39.068	3.957	2.571	6.091	< 0.001**
Multivariate analysis:							
TNM stage	2.204	0.548	16.142	9.058	3.091	26.539	< 0.001**
Differentiation degree	0.352	0.518	0.464	1.423	0.516	3.923	0.496
Lymph node metastasis	1.121	0.543	4.26	3.069	1.058	8.899	0.039*
DEK	1.416	0.422	11.272	4.121	1.803	9.42	< 0.001**

B – coefficient, SE – standard error, Wald – Wald statistic, HR – hazard ratio, CI – confidence interval. \* $P < 0.05$ , \*\* $p < 0.001$ .

### DEK overexpression independently predicts prognosis in ESCC

Univariate analysis revealed that ESCC cases highly expressing DEK had markedly reduced disease-free and 5-year survival rates in comparison with patients lowly expressing DEK. In addition, TNM stage, differentiation degree, and lymph node metastasis (LNM) also showed significant associations with disease-free and 5-year survival rates. Multivariate analysis indicated that high

TNM stage and LNM independently predicted poor prognosis in ESCC. It should be noted that high DEK expression was also confirmed to independently predict prognosis in ESCC (Table III).

### Discussion

Although significant associations of DEK with numerous cancers in humans have been reported, little is known about its effects in ESCC [28]. In this study, IHC analysis was performed to detect DEK

protein expression in ESCC samples and para-carcinoma tissue specimens. As shown above (Table I, Figure 1), DEK was ubiquitously distributed in the nucleus of ESCC cells, with the rate of DEK expression (71.7%) markedly increased compared to para-carcinoma (21.4%) and normal esophageal tissues (13.9%, both  $p < 0.001$ ). In agreement, the positive rate of DEK overexpression in ESCC tissues (57.5%) was markedly elevated compared with that in the para-carcinoma (11.4%) and normal esophageal samples (0%, both  $p < 0.001$ ). The result was consistent with other studies in solid tumors which demonstrated that DEK was overexpressed in cancerous cells, such as HCC cells, lung cancer cells, bladder cancer cells and colorectal carcinoma cells [7–9, 11, 27, 29]. These findings provide valuable support for DEK as a potential diagnostic biomarker in solid tumors, including ESCC.

Next, associations of DEK overexpression with clinical and pathological indexes in ESCC were assessed. As shown above (Table II), the expression level of DEK correlated with TNM stage and the degree of tissue differentiation. The rate of DEK overexpression was significantly elevated in advanced-stage (III–IV) ESCC patients (89.1%) compared with early-stage (I–II) patients (30.8%,  $p < 0.001$ ). Similarly, the rate of DEK overexpression was considerably increased in poorly differentiated esophageal cancer (85.1%) compared with moderately and well-differentiated cancers (39.7%,  $p < 0.001$ ). Several studies have also reported that DEK overexpression was significantly related to clinical prognostic parameters [23, 31–33]. Liu *et al.* reported that DEK expression level is considerably higher in invasive ductal breast cancer compared with normal breast tissue and associated with proliferation (Ki-67 levels) and histological grade, indicating that DEK might potentially be an indicator for early detection and prognosis [32]. Sun *et al.* reported that DEK overexpression was strongly related to histological grade and TNM stage which indicated poor prognosis and recurrence in patients with pancreatic ductal adenocarcinoma (PDAC) [31]. Riveiro-Falkenbach *et al.* demonstrated that DEK expression was significantly positive in malignant lesions of melanoma, especially in metastatic cases, and correlated with histological features of aggressiveness [23]. In HPV16+ oropharyngeal squamous cell carcinoma, DEK overexpression was associated with advanced tumor stage and increased risk of death [33]. Our study indicated that elevated DEK expression might be a useful biomarker for evaluating ESCC progression and aggressiveness. In an *in vivo* study, Matrká *et al.* found that DEK overexpression could stimulate gross esophageal tumor development and cause a trend toward esophageal hyperplasia by employing a DEK transgenic mouse model [28].

In this study, ESCC cases with highly expressing DEK showed markedly reduced survival compared with those displaying low levels (Figure 2). Multivariate survival analysis confirmed DEK overexpression as an independent predictive factor of poor survival in ESCC, alongside TNM stage and lymph node metastasis (Table III). The association of DEK overexpression with disease-free survival or survival rates was consistent with other studies which reported that increased DEK expression was clearly correlated with poor prognosis in other solid tumors [7, 31, 32]. Sun *et al.* demonstrated that patients with high DEK expression had a lower overall survival rate than those with low DEK expression [31]. Liu *et al.* found that DEK protein levels were remarkably reduced in breast carcinoma cases with  $< 3$ -year disease-free survival (DFS) compared with those showing  $\geq 3$ -year DFS [32]. Our previous study reported that DEK overexpression was significantly associated with portal vein invasion, tumor size and poor prognosis in HCC patients, showing that patients with high DEK expression had a shorter overall survival time than those with low expression [7].

In conclusion, based on the results obtained in the Cox regression model, DEK has been identified as a factor that is associated with reduced survival in both univariate analysis and multivariate analysis. Therefore, we can conclude that DEK expression is positively correlated with reduced survival in ESCC patients. Therefore, applying IHC in cancer tissues collected from ESCC patients to detect DEK expression would be helpful to evaluate the outcome after surgery. Our study has confirmed that DEK has potential to be an independent biomarker in predicting prognosis of ESCC patients. There are several limitations in the present study, which need to be stated. First of all, the sample size was limited. Secondly, the study was hospital-based, which may introduce selection bias of study subjects. Thirdly, we did not employ an animal model to investigate the impact of DEK on ESCC prognosis. Future investigations should be conducted to expand the sample volume among multi-center studies and test *in vivo* for understanding the straightforward role and mechanisms of DEK in ESCC malignancy.

### Conflict of interest

The authors declare no conflict of interest.

### References

1. Nassri A, Zhu H, Muftah M, Ramzan Z. Epidemiology and survival of esophageal cancer patients in an American cohort. *Cureus* 2018; 10: e2507.
2. Abnet CC, Arnold M, Wei WQ. Epidemiology of esophageal squamous cell carcinoma. *Gastroenterology* 2018; 154: 360-73.

3. Liang H, Fan JH, Qiao YL. Epidemiology, etiology, and prevention of esophageal squamous cell carcinoma in china. *Cancer Biol Med* 2017; 14: 33-41.
4. Kang K, Huang YH, Li HP, Guo SM. Expression of UCA1 and MALAT1 long-chain non-coding RNAs in esophageal squamous cell carcinoma tissues is predictive of patient prognosis. *Arch Med Sci* 2018; 14: 752-9.
5. Liang QL, Wang BR, Li ZY, Chen GQ, Zhou Y. Effect of TSLC1 gene on growth and apoptosis in human esophageal carcinoma Eca109 cells. *Arch Med Sci* 2012; 8: 987-92.
6. von Lindern M, Fornerod M, van Baal S, et al. The translocation (6;9), associated with a specific subtype of acute myeloid leukemia, results in the fusion of two genes, dek and can, and the expression of a chimeric, leukemia-specific dek-can mRNA. *Mol Cell Biol* 1992; 12: 1687-97.
7. Yi HC, Liu YL, You P, et al. Overexpression of DEK gene is correlated with poor prognosis in hepatocellular carcinoma. *Mol Med Rep* 2015; 11: 1318-23.
8. Zhou QC, Deng XF, Yang J, et al. Oncogene DEK is highly expressed in lung cancerous tissues and positively regulates cell proliferation as well as invasion. *Oncol Lett* 2018; 15: 8573-81.
9. Datta A, Adelson ME, Mogilevkin Y, Mordechai E, Sidi AA, Trama JP. Oncoprotein DEK as a tissue and urinary biomarker for bladder cancer. *BMC Cancer* 2011; 11: 234.
10. Han S, Xuan Y, Liu S, et al. Clinicopathological significance of DEK overexpression in serous ovarian tumors. *Pathol Int* 2009; 59: 443-47.
11. Lin L, Piao J, Gao W, et al. DEK over expression as an independent biomarker for poor prognosis in colorectal cancer. *BMC Cancer* 2013; 13: 366.
12. Smith EA, Gole B, Willis NA, et al. DEK is required for homologous recombination repair of DNA breaks. *Sci Rep* 2017; 7: 44662.
13. Piredda ML, Catalano G, Ciardi C, et al. Identification of a potential topoisomerase II "hotspot" DNA region in the DEK gene in two t(6;9)-positive therapy-related myeloid neoplasms. *Ann Hematol* 2017; 96: 155-7.
14. Deutzmann A, Ganz M, Schonenberger F, Vervoorts J, Kappes F, Ferrando-May E. The human oncoprotein and chromatin architectural factor DEK counteracts DNA replication stress. *Oncogene* 2015; 34: 4270-7.
15. Kavanaugh GM, Wise-Draper TM, Morreale RJ, et al. The human DEK oncogene regulates DNA damage response signaling and repair. *Nucleic Acids Res* 2011; 39: 7465-76.
16. Yamazaki H, Iwano T, Otsuka S, et al. Sirna knockdown of the DEK nuclear protein mrna enhances apoptosis and chemosensitivity of canine transitional cell carcinoma cells. *Vet J* 2015; 204: 60-5.
17. Karam M, Thenoz M, Capraro V, et al. Chromatin redistribution of the DEK oncoprotein represses htert transcription in leukemias. *Neoplasia* 2014; 16: 21-30.
18. Nakashima T, Tomita H, Hirata A, et al. Promotion of cell proliferation by the proto-oncogene DEK enhances oral squamous cell carcinogenesis through field cancerization. *Cancer Med* 2017; 6: 2424-39.
19. Liu G, Xiong D, Zeng J, et al. Prognostic role of DEK in human solid tumors: a meta-analysis. *Oncotarget* 2017; 8: 98985-92.
20. Liu K, Feng T, Liu J, Zhong M, Zhang S. Silencing of the DEK gene induces apoptosis and senescence in caski cervical carcinoma cells via the up-regulation of NF-kap-pab p65. *Biosci Rep* 2012; 32: 323-32.
21. Adams AK, Hallenbeck GE, Casper KA, et al. DEK promotes HPV-positive and -negative head and neck cancer cell proliferation. *Oncogene* 2015; 34: 868-77.
22. Wise-Draper TM, Morreale RJ, Morris TA, et al. DEK proto-oncogene expression interferes with the normal epithelial differentiation program. *Am J Pathol* 2009; 174: 71-81.
23. Riveiro-Falkenbach E, Ruano Y, Garcia-Martin RM, et al. DEK oncogene is overexpressed during melanoma progression. *Pigment Cell Melanoma Res* 2017; 30: 194-202.
24. Martinez-Useros J, Rodriguez-Remirez M, Borrero-Palacios A, et al. DEK is a potential marker for aggressive phenotype and irinotecan-based therapy response in metastatic colorectal cancer. *BMC Cancer* 2014; 14: 965.
25. Logan GE, Mor-Vaknin N, Braunschweig T, et al. DEK oncogene expression during normal hematopoiesis and in acute myeloid leukemia (AML). *Blood Cells Mol Dis* 2015; 54: 123-31.
26. Ou Y, Xia R, Kong F, et al. Overexpression of DEK is an indicator of poor prognosis in patients with gastric adenocarcinoma. *Oncol Lett* 2016; 11: 1823-8.
27. Liu X, Qi D, Qi J, et al. Significance of DEK overexpression for the prognostic evaluation of non-small cell lung carcinoma. *Oncol Rep* 2016; 35: 155-62.
28. Matrka MC, Cimperman KA, Haas SR, et al. DEK overexpression in murine epithelia increases overt esophageal squamous cell carcinoma incidence. *PLoS Genet* 2018; 14: e1007227.
29. Wang X, Lin L, Ren X, et al. High expression of oncoprotein DEK predicts poor prognosis of small cell lung cancer. *Int J Clin Exp Pathol* 2014; 7: 5016-23.
30. Piao J, Shang Y, Liu S, et al. High expression of DEK predicts poor prognosis of gastric adenocarcinoma. *Diagn Pathol* 2014; 9: 67.
31. Sun J, Bi F, Yang Y, et al. DEK protein overexpression predicts poor prognosis in pancreatic ductal adenocarcinoma. *Oncol Rep* 2017; 37: 857-64.
32. Liu S, Wang X, Sun F, Kong J, Li Z, Lin Z. DEK overexpression is correlated with the clinical features of breast cancer. *Pathol Int* 2012; 62: 176-81.
33. Smith EA, Kumar B, Komurov K, et al. DEK associates with tumor stage and outcome in HPV16 positive oropharyngeal squamous cell carcinoma. *Oncotarget* 2017; 8: 3414-26.