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CDC20, TOP2A and NEK2 Expression in Esophageal Squamous Cell Carcinoma and Its Clinical Significance

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ABSTRACT

Objective: to study the expression and clinical significance CDC20, TOP2A, NEK2 esophageal squamous cell carcinoma. **Methods:** To select 70 patients with esophageal squamous cell carcinoma, Between August 2018 - August 2020, All intraoperative pathological specimens, A group -35 cases), Cancer tissue, B group, adjacent tissues), two groups of CDC20, TOP2A, NEK 2 expression were detected and analyzed by immunohistochemistry and semi-quantitative reverse transcription polymerase chain reaction -RT-PcR) assay. **Results:** the values of CDC20, TOP2A, NEK2 expression level in A group were significantly higher than those in B group -P<0.05). The expression level CDC20, TOP2A, NEK2 esophageal squamous cell carcinoma was positively correlated with TNM stage and lymphatic metastasis, and negatively correlated with tumor differentiation. **Conclusion:** CDC20, TOP2A, NEK2 high expression level directly affects the metastasis, recurrence and prognosis of esophageal squamous cell carcinoma. The combination of three indexes can accurately evaluate the pathological status of patients with esophageal squamous cell carcinoma and help to judge the prognosis of patients accurately.

1. Introduction

Esophageal squamous cell carcinoma is a malignant tumor of digestive tract with high clinical incidence. According to the World Health Organization report, esophageal squamous cell carcinoma in the world ranked eighth, mortality ranked sixth. In our country, phase the five-year survival rate in patients with esophageal squamous cell carcinoma is between 15% and 25%, according to the study ^[1]. With the development of modern medical research on the biological mechanism

and molecular mechanism of esophageal squamous cell carcinoma, the gene and protein development mechanism related to this disease has made great progress. Related studies have confirmed that TOPA2 expression directly affects tumor cell apoptosis, while cell division cyclin 20-CDC20) has a positive effect on tumor cell infiltration. Mitotic regulatory kinase 2-NEK2) was significantly abnormal in pathological tissues of end-stage tumor patients. Expression and clinical significance CDC20, TOP2A, NEK2 esophageal squamous cell carcinoma were discussed.

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2. Information and Methodology

2.1 General Information

The patients with esophageal squamous cell carcinoma were selected from 70 cases of esophageal squamous cell carcinoma. The interval was August 2018 - August 2020. All the samples were collected by intraoperative pathology, A group -35 cases, cancer tissue), B group -35 cases, adjacent tissue).

Among them, Male patients 56, female patients 24; Between 45 -72, Mean (-62.15+2.25) years; TNM staging:12 cases in phase I, A total of 33 cases in phase II, A total of 23 cases in phase III, Phase IV totalled 12 cases; Tumor differentiation: a total of 42 cases of middle and high differentiation, A total of 38 cases of low differentiation; Lymphatic metastasis: a total of 33 cases, There were 47 cases without lymphatic metastasis. Inclusion criteria:1 all included patients did not carry out radiotherapy and chemotherapy before operation; -2) indication of surgical resection; 3. Complete case examination data; Know the contents of the test and sign the agreement. Exclusion criteria:1 with severe complications; Preoperative radiotherapy and chemotherapy; 3 Poor coordination. Above data is balanced -P>0.05).

2.2 Method

Routine formaldehyde -10% concentration) was used to fix all samples. The fixation time was controlled between 4 -6 h. Gradient dehydration, tissue wax immersion, paraffin embedding, sectioning, immunohistochemical S-P method were used to observe and evaluate the expression gray value of CDC20, TOP2A, NEK2 in esophageal squamous cell carcinoma. Results: two experienced pathologists were arranged to observe tumor cells, nuclei or cytoplasm by high magnification (×400) under the condition of double blind method. Once yellow or brown granules were found, positive cells could be determined. Select 5 visual fields for each specimen, And 100 tumor

cell counts per field of vision, Total 500, The statistical ratio of positive cells was calculated accurately. Positive criteria: positive cell rate of 10% and above; Negative criteria: positive cell rate less than 10%. Semi-quantitative reverse transcription polymerase chain reaction -RT-PCR) to accurately detect CDC20, TOP2A, NEK2 expression factors in the pathological tissue of patients, The extraction and DEPC preparation of gene RNA according to the standard protocol of the TrizolRNA kit, MRNA integrity was identified by agarose gel electrophoresis. That is, the practical ABI7500 real-time quantitative PCR instrument, Can achieve the purpose of specimen gene amplification, After uVIpro ultraviolet gel imaging and analysis system observation, scanning, photography and other series of operations, The CDC20, TOP2A, NEK2 and β-actin expression intensity in the picture were observed and analyzed.

2.3 Statistical Analysis

The experimental data are processed in parallel SPSS19.0 new model building, in which the qualitative data are expressed as percentage (%) and the test χ is used²The quantitative data showed that the results were statistically significant P<0.05.

3. Results

3.1 CDC20, TOP2A, NEK2 Expressional Characteristics

S-P results showed that the cancer cells were nest-like distribution, accompanied by irregular cell series, abnormal cells, nuclear mitosis, and obvious positive particles in the cytoplasm.

3.2 Analysis of CDC20, TOP2A, NEK2 Expression in Different Esophageal Tissue Samples

The values of CDC20, TOP2A, NEK2 expression level in A group were significantly higher than those in B group -P<0.05) (See Table 1).

Table 1. Analysis of CDC20, TOP2A, NEK2 expression in different esophageal tissue samples -±s)

Group	CDC20		TOP2A		NEK2	
	mRNA Relative Expression Coefficient	The gray level of protein expression	mRNA Relative Expression Coefficient	The gray level of protein expression	mRNA Relative Expression Coefficient	The gray level of protein expression
A group	1.259±0.246	15.259±4.258	0.668±0.118	54.892±1.976	0.856±0.176	1.235±0.068
B group	0.967±0.168	10.072±4.224	0.516±0.084	42.772±1.617	0.702±0.151	0.865±0.032
t	5.799	5.116	6.208	28.083	3.929	29.127
p	0.000	0.000	0.000	0.000	0.000	0.000

Table 2. CDC20, TOP2A, NEK2 Expression and clinicopathological features and correlation analysis

Clinical data	Number of cases	CDC20 positive	χ^2	P	TOP2A	χ^2	P	NEK2	χ^2	P
TNM staging			8.903	0.003		6.612	0.010		8.762	0.002
I	12	4 (33.33)			3 (25.00)			2 (16.67)		
II	33	20 (60.61)			19 (57.58)			17 (51.52)		
III	23	18 (78.26)			18 (78.26)			20 (86.96)		
IV	12	11 (91.67)			10 (83.33)			12 (100.00)		
Tumor differentiation			5.038	0.025		6,737	0.009		5.402	0.020
Medium High Differentiation	42	28 (66.67)			25 (59.52)			29 (69.05)		
Low differentiation	38	32 (84.21)			30 (78.95)			20 (52.63)		
lymphatic metastasis			8.202	0.004		4.369	0.037		4.716	0.029
Yes	33	26 (78.79)			24 (72.73)			25 (75.76)		
No	47	27 (57.44)			27 (57.44)			28 (49.12)		

3.3 CDC20, TOP2A, NEK2 Expression and Clinicopathological Features and Correlation Analysis

The expression level CDC20, TOP2A, NEK2 esophageal squamous cell carcinoma was positively correlated with TNM stage and lymphatic metastasis, and negatively correlated with tumor differentiation (See Table 2).

4. Discussion

CDC20 cell cyclin plays a key role in the normal mitosis of cells, mainly in the -G stage of cell mitosis, The effective regulation of chromosome DNA division and replication in M cells and the active promotion of positive regulators in late complex / periodic APC/C. Studies have confirmed that the occurrence of CDC20 abnormal expression is likely to cause mitosis errors, and will lead to the wrong expression of some cancer genes and tumor suppressor gene mutations or even disappear. Abnormal CDC20 expression can create better conditions for the proliferation and self-repair of cancer cells, leading to the risk of uncontrolled tumor inhibition in cancer patients greatly increased [2]. In addition, CDC20 can slow down the apoptosis rate of tumor cells and play an important role in tumor progression. can be seen that CDC20 as a new target for tumor therapy is highly feasible. According to relevant studies, esophageal squamous cell carcinoma is closely related to molecular biological factors, including activation / inactivation of proto-cancer / tumor suppressor gene, repair of regulatory DNA and dysfunction of regulatory proteins that maintain gene stability. TOP2A is an important regulatory enzyme in the nucleus, second only to histone protease. Its mechanism

is to control and change the topological state of DNA transcriptional network and the transcription of DNA. It has good effect on the function regulation of chromosome condensation and chromatid separation [3]. Studies have shown that TOPA2 can promote the formation of TOP-DNA-AMPPNP complexes and participate effectively in cell mitosis by shearing DNA,. NEIK2 can establish bipolar spindle quickly by regulating the central body to copy, separate and mature correctly. At present, it has been proved that NEK2 expression is high in many tumors and malignant glioma tissues, and with the progression of malignant tissues, the expression level of malignant tissues increases significantly [4]. Abnormal NEK2 expression is highly likely to cause abnormal changes in centrosome structure, which in turn leads to functional defects, which will lead to the overall stability of infected genes, induce malignant transformation of cells and participate in tumor metastasis and infiltration.

The results showed that CDC20, TOP2A, NEK2 and other expression factors in esophageal squamous cell carcinoma showed a high level, which showed an increasing trend compared with adjacent tissues, and the data between groups were significantly different, and there was a positive correlation with TNM stage, tumor differentiation, lymphatic metastasis and other related factors. CDC20, TOP2A, NEK2 directly affects the pathological progression and metastasis of esophageal squamous cell carcinoma. Therefore, the abnormal expression of CDC20, TOP2A, NEK2 is beneficial to the prediction and evaluation of invasion, metastasis and recurrence of esophageal squamous cell carcinoma, and with the aggravation of TNM stage, the expression of its indexes is obviously on the rise. By CDC20, TOP2A,

NEK2 joint examination, it can provide reliable reference for the evaluation of the deterioration and development mechanism, stage and differentiation degree of esophageal squamous cell carcinoma, and improve the clinical diagnosis and treatment effect of esophageal squamous cell carcinoma. Combined CDC20, TOP2A, NEK2 therapy is of great significance for the evaluation of pathological status and prognosis of esophageal squamous cell carcinoma.

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